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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 9 1953

THE PREMENSTRUAL SYNDROME

BY

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"Premenstrual tension," as it has hitherto been called, is the commonest of the minor endocrine disorders. The fact that a large number of women suffer from a variety of symptoms, unpleasant at their mildest and at their severest incapacitating, during the ultimate seven to ten days of the menstrual cycle is well known; but in this country very little has been done to alleviate their distress. This is partly due to the attitude of the patients. Just as, before the days of stilboestrol, women in general accepted the unpleasant symptoms of "the change of life" as a necessary part of the business of being a woman, so still they pass through one week of discomfort in every month, usually without complaining to their doctors but not necessarily without disturbing the tranquillity of their homes. The frequency of the condition is testified to by the fact that in one American factory, employing 1,500 women, 36% applied for treatment in the premenstrual phase (Bickers and Woods, 1951). Israel (1938) stated that symptoms of the kind to be described occur in 40% of otherwise healthy women. It is, we are convinced, equally common in this country, and it is therefore curious that, although many papers on the subject have been published in the U.S.A., we have been able to trace only one in a British journal (Singh *et al.*, 1947), which did not refer to British patients.

The term "premenstrual tension" is unsatisfactory, for tension is only one of the many components of the syndrome. Its use has commonly led to a failure to recognize the disorder when tension is absent or is overshadowed by a more serious complaint. We have preferred to use the term "premenstrual syndrome," but as our investigation has progressed it has become clear that this term also is unsatisfactory. Though the syndrome most commonly occurs in the premenstrual phase, similar symptoms occasionally occur at the time of ovulation, in the early part of the menstrual phase, and even, rarely, in the first day or two after the flow has ceased. The term "menstrual syndrome," though correct, for in each individual the symptoms recur at monthly intervals, may wrongly create the impression that they occur only during menstruation. We have finally decided to retain the term "premenstrual syndrome" in the full realization of its imperfection. The full elucidation of its cause may later suggest a more appropriate and more accurate nomenclature.

The Literature

The first description of the syndrome is that of Frank (1931). He records a condition of indescribable tension and a desire to find relief by foolish actions difficult to restrain. There were often severe headaches and palpable oedema, especially of the face, hands, and feet, accompanied by oliguria and an increase in weight. Sometimes there were diffuse spontaneous subcutaneous haemorrhages, asthma, and, in rare instances, epileptiform seizures. All symptoms were rapidly relieved at the onset of the menstrual flow, but recurred at varying times as the end of the cycle drew near. The condition of the patients became worse if the onset of the flow was delayed. Soon other symptoms with a similar periodicity were observed, including a remarkable degree of oedema, which caused, in two cases described by Thomas (1933), a gain in weight of 12 to 14 lb. (5.4 to 6.4 kg.), relieved on the first day of menstruation by a diuresis of 4.5 litres, continued on the succeeding days.

Sweeny (1934) described tightness of the clothing and stiffness of the hands, and found that 30% of 42 healthy women gained 3 lb. (1.4 kg.) or more in the premenstrual phase. Puech (1942) laid stress on premenstrual asthmatic attacks, rhinorrhoea, fever, and lumbar pain. Israel (1938) recorded ulcerative stomatitis and transient nymphomania. Of 38 patients described by Gray (1941), 5 had nymphomania and 15 some form of "psychosexual disorder." Rubenstein (1942) stressed the incapacitating headache common at this time, in one patient associated with abnormal hunger; and Morton and McGavack (1946) were inclined to associate this with hypoglycaemia. Morton (1946) drew attention to the frequent association of the other symptoms with pain in the breasts.

Stieglitz and Kimble (1949) found, in a series of 67 patients, that 68% suffered from emotional instability, 65% from headache (in 12 instances amounting to typical migraine), 50% from backache, 47% from depression, 36% from aching in the thighs, and 9% from "bloating" of the abdomen. Of Morton's (1950) 29 patients, all had transient emotional instability, and the majority had pain in the breasts, increased appetite, lower abdominal pain, abdominal bloating, and gain in weight. Almost half had palpable oedema, about one-third had

menstrual irregularity, and a few had nausea and vomiting, increased sexual desire, and pruritus vulvae. One patient had headache, papilloedema, vertigo, and projectile vomiting of a degree suggesting an intracranial tumour. Cooke (1945) reported that 84% of crimes of violence by women occurred during or immediately before the menses. Morton *et al.* (1952), in a study of prison inmates, found that crimes of violence had been committed in 62% of the cases in the premenstrual week, in 19% at mid-cycle, in 17% during menstruation, and in 2% after the end of menstruation.

Analysis of 84 Cases of Premenstrual Syndrome

This series contains the histories of 84 cases of premenstrual syndrome which were treated with ethisterone and/or progesterone, and an analysis of results of treatment in 78 cases. All cases were seen between 1948 and 1952 and attended for a follow-up interview in 1952. Of the 84 patients in the series, 16 were first seen in hospital by R. G. Most of the remainder were collected by K. D. in her own practice (which has a National Health panel of 5,000), after the successful treatment of her own case, and were referred to R. G. Sixteen patients were referred to K. D by her fellow general practitioners.

All the cases had attacks of various symptoms, which occurred during the premenstrual phase, during menstruation or ovulation, or at the time of a missed period, and all cases were symptom-free at other times. All cases included in the series had experienced attacks during each of the last three menstrual cycles; thus any chance coincidence between the attack and menstruation was eliminated. Any case in which the time relationship was not definite was temporarily excluded, the patients being treated symptomatically and asked to keep a calendar.

The "presenting" and other symptoms which occurred during attacks are shown in Table I. "Presenting symptoms" always occurred with each attack, but the other symptoms were not necessarily present with each attack. The site of the premenstrual headache in the 58 cases was: bifrontal, 19; hemicranial, 13; bitemporal, 4; between eyes, 1; behind eyes, 1; over one eye, 12; occipital, 4; vertical, 1; not recorded, 3. In 22 cases the severity necessitated rest in bed, and in 10 cases concomitant symptoms made a diagnosis of migraine inevitable. The visual symptoms noted in these 10 cases of migraine were: photophobia, 4; mistiness, 1; hemianopia, 2; burning pain, 2; flashes of light, 1. Table II shows the sites of premenstrual rheumatism, and Table III the types of skin and mucous lesions.

TABLE I.—*Symptoms*

Symptom	Presenting		Other		Total	
Headache	53	63·1%	5	6·0%	58	69·5%
Nausea	2	2·4%	23	27·4%	25	29·7%
Irritability	2	2·4%	3	3·6%	5	6·0%
Depression	1	1·2%	4	4·8%	5	6·0%
Lethargy	—	—	11	13·1%	11	13·1%
Vertigo	1	1·2%	8	9·5%	9	10·6%
"Rheumatism"	5	6·0%	9	10·6%	14	16·7%
Skin and mucosal lesions	9	10·6%	2	2·4%	11	13·1%
Oedema	1	1·2%	4	4·8%	5	6·0%
Rhinorrhoea	3	3·6%	3	3·6%	6	7·2%
Asthma	4	4·8%	—	—	4	4·8%
Epilepsy, petit mal	3	3·6%	1	1·2%	5	6·0%
" grand mal	—	—	1	1·2%		
Mastalgia	—	—	2	2·4%	2	2·4%

TABLE II.—*Sites of Premenstrual Rheumatism*

	Presenting Symptom	Other Symptoms	Total
Shoulder	1	1	2
Knees	—	1	1
Feet	2	—	2
Sciatica	2	—	2
Lumbago	2	4	6
Hips	—	1	1
Thighs	—	2	2
Neck	—	1	1
Hands	1	—	1
Total	8*	10	18

* Some patients mentioned more than one site.

TABLE III.—*Types of Premenstrual Skin and Mucous Lesions*

Type	Site	Presenting	Other Symptoms	Total
Acne	Face	1	1	2
	Shoulders and back	2	—	2
Acrocyanosis	Toes	1	—	1
Styes	Eyes	1	—	1
*Seborrhoeic dermatitis	Cubital fossa	—	1	1
*Dry eczema	Neck	1	—	1
*Erythema multiforme	Lower lip	1	—	1
"Glossitis"	Tongue	2 (sisters)	—	2
Total		9	2	11

* Diagnostic label attached by dermatologist.

In view of the suggestion of Salmon (1947) that the onset may be related to sexual dissatisfaction, a search was made for this and other possible psychological causes. No case of sexual maladjustment was found. The incidents (not necessarily significant) associated with the onset of symptoms in our 84 cases were as follows: puberty, 27; childbirth, 15; menopause, 14; widowed, 1; divorced, 1; mumps oophoritis, 1; thyroidectomy, 1; marriage, 3; unknown, 21.

TABLE IV.—*Duration of History of Regular Attacks of Premenstrual Syndrome*

Under 1 year	18	21·4%
1–5 years	35	41·6%
6–10 ,,	10	12·0%
11–15 ,,	9	10·6%
16–20 ,,	7	8·4%
Over 20 years	5	6·0%
	84	100

Menstrual History

Fig. 1 shows the usual time of onset of the attack. In this series 70 patients expected attacks in the premenstrual week, 9 at the onset of menstruation, and 4 during menstruation.

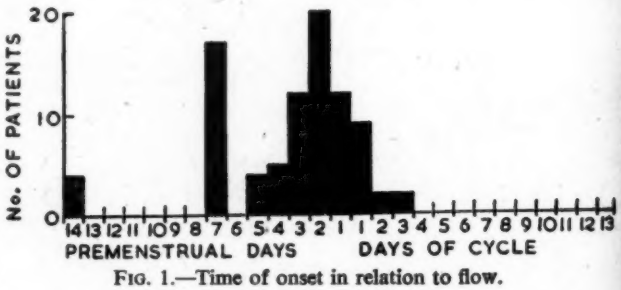

FIG. 1.—Time of onset in relation to flow.

One patient had regular attacks only at ovulation, and 3 had bimensual attacks at ovulation and premenstrually. One of these had ovulatory bleeding. When, as at puberty and in the climacteric, periods are missed, the attacks nevertheless occur on the expected dates. Table V and Fig. 2 show the age at which the first menstrual loss occurred. This was normal in 72 cases, with only 2 cases (2.4%) occurring at the early age of 10 years, and only 5 cases (6%) occurring later than the normal time of onset (arbitrarily assumed to be 11 to 16 years).

Table VI shows the duration of menstrual loss. In only three cases was it abnormally short (two days), and in only one abnormally long (10 days).

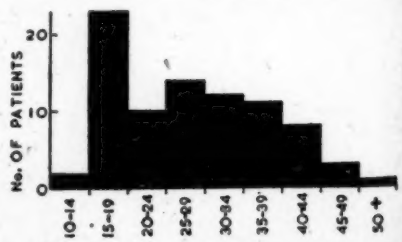

FIG. 2.—Age at onset of symptoms.

TABLE V.—*Age at First Menstrual Period*

	Normal Age Limit										Total
Years:	10	11	12	13	14	15	16	17	18	?	
Cases	2	6	10	19	19	12	6	3	2	5	84
% ..	2·4	7·1	12·0	22·6	22·6	14·2	7·1	3·6	2·4	6·0	100

TABLE VI.—*Average Duration of Menstrual Loss*

Days:	1	2	3	4	5	6	7	8	9	10	?	Total
Cases	—	3	11	17	23	14	12	—	—	1	3	84
% ..	—	3·6	13·1	20·2	27·4	16·7	14·2	—	—	1·2	3·6	100

TABLE VII.—*Length of Menstrual Cycle*

	Normal Length			
Days:	Under 21	21–30	31–42	Irregular	Total
Cases	1	78	4	1	84
%	1·2	92·8	4·8	1·2	100

Table VII, giving the length of the usual menstrual cycles, shows that the cycle exceeded the normal 30 days in four cases only—in women aged 16, 17, 30, and 31 years. The series is conspicuous for the normality of the menstrual history. An irregular cycle had been present in one woman of 49 for twelve months, and presumably heralded the climacteric. In one woman of 27 ovulatory bleeding had occurred regularly at the 14th to 15th day of a 28-day cycle, and she also suffered from migraine at this time. In this respect our experience differs from that of Singh *et al.* (1947), who found a high incidence of abnormal menses.

Two patients had "slight" dysmenorrhoea—that is, the patient had some discomfort relieved by simple analgesics, but the pain was not sufficient to interfere with normal work or necessitate lying down. The other 82 patients had no dysmenorrhoea. One case of associated severe dysmenorrhoea has since been observed.

Effect of Pregnancy

TABLE VIII.—*Parity of Series*

	Our Series	Registrar-General's Figures (Ages 15–45)
Single women	13 (15·5%)	43·2%
Married, no children ..	13 (15·5%)	13·3%
,, 1 child	25 (29·6%)	18·3%
,, 2 children	11 (13·1%)	14·4%
,, 3 ,, ...	13 (15·5%)	5·7%
,, 4 ,, ...	5 (6·0%)	2·7%
,, 5 or more children	4 (4·8%)	2·4%

Table VIII shows the parity of the series. The patients conceived easily and none had required medical advice on account of infertility. Most had their children in close succession, and all but two married women who had not had a child in the previous twelve months stated that they were practising some form of contraception. Three normal deliveries and one miscarriage at ten weeks occurred during treatment.

TABLE IX.—*Health After First Trimester of Pregnancy*

More energetic, symptom-free	36 (62·1%)
Symptom-free	18 (31%)
Symptoms (depressed 2, migraine 1, asthma 1) ..	4 (6·9%)
	58 (100)

Table IX shows the state of health of the patient after the first trimester. After the third month of pregnancy the premenstrual symptoms ceased in all but four patients, and 36 patients reported feeling more energetic than usual.

Toxaemia occurred in 11 of 58 parous women and complicated 21 of 128 pregnancies, thus accounting for the following obstetrical complications: surgical induction, 12; caesarean section, 4; forceps, 2; stillbirth, 3; sterilization, 1.

In 5 out of 11 cases the premenstrual syndrome began after the pregnancy complicated by toxaemia. The possible association between the syndrome and toxaemia is under further investigation.

Effect of Childbirth

In all cases in which the syndrome existed before pregnancy the attacks occurred with increased severity at the first menstruation after childbirth. Three patients with migraine had an attack during the puerperium; 15 dated the onset of regular attacks from childbirth.

In seven cases childbirth was followed by increasing weight and lethargy in addition to the premenstrual syndrome, a condition easily misdiagnosed as myxoedema, but which responded to ethisterone or progesterone therapy.

In view of the frequency of the syndrome no sound conclusions about familial incidence can be drawn from so small a series. It may, however, be worthy of note that the mothers of 29 of our patients had suffered from migraine: of these, 14 suffered from attacks which were related to menstruation and which ceased at the menopause. Seven of our patients reported similar conditions in their sisters, in five instances in relation to menstruation. One patient reported that her father suffered from migraine. Two patients who were cousins were able to trace premenstrual migraine in four generations.

Is Water Retention the Cause of the Syndrome?

That the symptoms are due to water retention is strongly suggested by the oliguria and gain in weight which announces their arrival and the diuresis and loss of weight which accompanies their relief at, or soon after, the onset of menstruation. To the observations already quoted may be added those of Thorn, Nelson, and Thorn (1938), who found a premenstrual gain in weight of more than 1 kg. in 48% of healthy women, and, be it noted, a mid-menstrual gain in 76%. They showed that at neither time was the gain attributable to increased intake of food, an important point in view of the increased appetite occasionally reported. Morton (1950) found that in his series of cases of "premenstrual tension" a higher proportion (52%) gained weight and that 45% had pitting oedema. Bickers and Woods (1951) found a good correlation between the gain in weight and the severity of the symptoms, and reproduced them by injections of "pitressin." Relief of the symptoms by various diuretic measures has been reported. Greenhill and Freed (1940) claimed success in all their patients treated with ammonium chloride and a diet low in sodium, and in a later and larger series (Greenhill and Freed, 1941) in 34 patients out of 40. Thorn and Emerson (1940) were successful with a diet low in sodium and high in potassium. Stieglitz and Kimble (1949), in order to avoid the chloride ion, preferred ammonium nitrate and obtained relief in 91% of their patients. Argonz and Abinzano (1950) treated 30 patients with large doses of vitamin A because of its reported diuretic effect, and claimed success in every case. Bickers and Woods (1951) relieved all symptoms with the new diuretic pyralamine-8-bromotheophylline, which reduced the average gain of weight from 5.2 to 1.4 lb. (2.4 to 0.6 kg.). Their results were less good with ammonium chloride, which reduced the gain only to 4.3 lb. (2 kg.). Vainder (1951) was successful in 153 cases treated with "pyrabom" (pyralamine-8-bromotheophylline).

Nevertheless, it is necessary to be on guard against too ready an explanation of the syndrome *solely* by water retention. Thorn, Nelson, and Thorn (1938), as we have seen, found that a gain in weight occurred more often at mid-cycle than in the premenstrual phase. Similar symptoms do sometimes occur at the time of ovulation, but they are far less common. Thorn and Emerson (1940) were disposed to explain this by the experimental fact that progesterone and oestradiol both have the capacity to cause water retention, and that, whereas only oestradiol is operative at mid-cycle, both are present before menstruation; but, for reasons which will later be obvious, this explanation is not

acceptable. In our series, symptoms occurred at mid-cycle in only four cases. Such women usually have two attacks, and sometimes these last long enough to merge with each other, especially when the cycle is short and the gap between menstruation and ovulation therefore also short. One unfortunate Irishwoman complained: "I only feel well when I am poorly." If we include mastalgia with the other symptoms we can assure ourselves that a factor other than water retention is involved. Greenhill and Freed (1941) noted that this symptom, alone in the syndrome, was not improved by dehydration, a fact which we have repeatedly confirmed.

Moreover, observation of a patient by one of us in 1938 (Fig. 3) suggests that a factor other than water retention

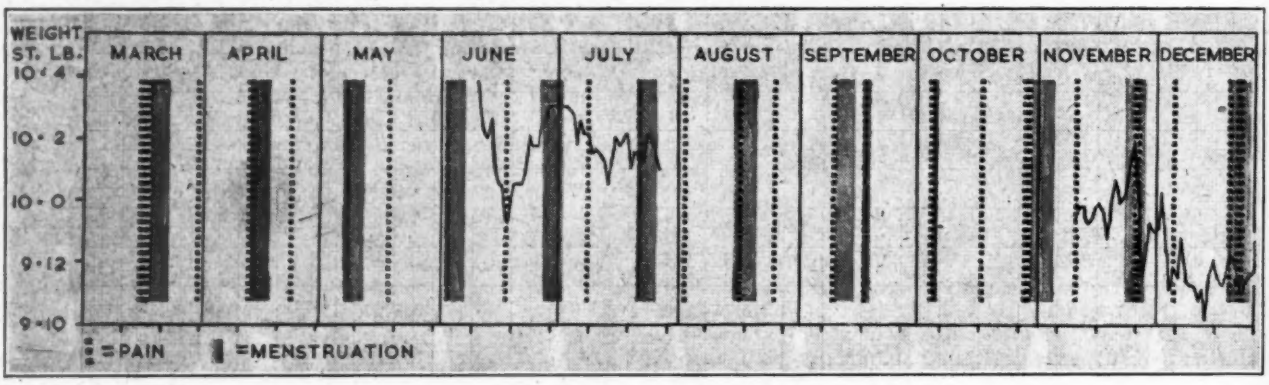

FIG. 3.—Occurrence of pain in relation to 11 menstrual cycles, together with weight changes during four cycles in a patient.

may sometimes be involved. She complained of attacks of migraine, occurring usually at intervals of a fortnight. She was intelligent and co-operative, and kept careful notes of her symptoms over a period of 11 cycles. During four cycles she plotted her weight day by day. These 11 cycles varied in length from 24 to 27 days. The attacks were of two kinds, occurring either during the interval or near the beginning of menstruation. The intermenstrual attacks, which all lasted for one day only, occurred nine times on the 14th or 15th days before menstruation. The two exceptions occurred on the 10th day before (when, uniquely in this study, no menstrual attack succeeded it) and on the 17th day before (when, again uniquely, it was accompanied by uterine haemorrhage and succeeded by a scanty menstrual flow). The menstrual attacks occurred in 10 cycles. They varied in length from one to three days, and their onset varied between the third day before the beginning of the flow to the second day after the beginning of the flow, in this way differing from the majority, in which all attacks were premenstrual.

It is important to observe that in the cycle in which there was an intermenstrual but no premenstrual attack, the weight dropped sharply by over 4 lb. (1.8 kg.) in the first half of the intermenstruum (the attack occurring at the nadir) and rose again by almost 4 lb. (1.8 kg.) in the second half (without any attack at the zenith). In the succeeding cycle weight changes were far less obvious and bore no relation to the attacks. Later in the series of cycles, one was observed in which the intermenstrual attack occurred before the nadir, though the premenstrual attack occurred at the zenith, and one in which an attack occurred intermenstrually before the nadir and premenstrually without a significant rise. Such observations enjoin some caution in assuming that water retention is the sole cause of intermenstrual and premenstrual or early menstrual migraine.

Another difficulty to be overcome arises from the reported effects of sterols in treatment. Oestrogens, androgens, and progestogens all have the property of causing water retention (Thorn and Engel, 1938; Kenyon *et al.*, 1940). Thorn, Nelson, and Thorn (1938) estimated that the relative potencies of the common sterols in this respect were, represented in "dog units," oestradiol 700, progesterone 400, oestrone 200–300, pregnanediol 140, testosterone 80, and testosterone propionate 25. Despite this, as we shall see, there is ample evidence of the effectiveness in treatment of progesterone, testosterone, testosterone propionate, and methyltestosterone. Still more surprising is the statement of Chiray *et al.* (1940) and Rubenstein (1942) that occasional cases respond to oestrogens, a claim we have been unable to confirm. Moreover, Singh *et al.* (1947) were able to induce attacks with oestrogens.

Though at first sight the water-retaining properties of progesterone and testosterone appear incompatible with their success in treatment, a hypothetical explanation may be suggested. The effects of progesterone on the excretion of oestradiol may more than counterbalance its weaker direct effect on water metabolism. That progesterone has this effect is shown by the observations of Smith and Smith (1931, 1938), which have been amply confirmed (Burrows, 1945).

Why Does Water Retention Occur?

The fact that two peaks of oestradiol secretion occur in each normal menstrual cycle—one at the time of ovulation and one in the premenstrual phase—suggests a hypothetical explanation of the retention of water at these times. That oestrogens are capable of causing water retention is well known, especially from the observations of Zuckerman and his colleagues (Krohn and Zuckerman, 1937; Aykroyd and Zuckerman, 1938; Zuckerman *et al.*, 1938).

Direct evidence of an excess of oestrogens at the time of the occurrence of symptoms is of doubtful validity. Frank (1931) and Frank *et al.* (1934), it is true, claimed that their patients' blood contained twice the normal amount of "ovarian hormone," and that after the relief of symptoms by *x* rays applied to the ovaries the ovarian hormone level became normal; but the difficulties inherent in the estimation of ovarian hormones in blood make it necessary to accept the statement with reserve. Morton found that vaginal smears were suggestive of excessive oestrogenic activity. On the other hand, Frank's suggestion of a high renal threshold for oestrogens was found by Israel (1938) in fewer than half his patients, which led him to suggest that the cause of the trouble was not so much a high level of oestradiol as a lack of antagonism by progesterone.

The concept of an abnormally high oestradiol/progesterone ratio has much in its support. Greenblatt (1940) contested the suggestion because in most of his patients he found a normal progestational pattern in their endometria and a normal excretion of pregnanediol; though he also noted a deficient excretion of oestrogens. Gray (1941) failed to find any correlation between the premenstrual syndrome and anovular cycles, and in the series reported by Bickers and Woods (1951) the basal temperature curve was invariably biphasic and the endometrial pattern progestational. Provenzano (1944) found a normal pattern in 12 out of 15 patients. It should, however, be pointed out that the hypothesis that the cause of the syndrome is an abnormally high

oestradiol/progesterone ratio does not at all depend on the demonstration of a consistently high level of the former or low level of the latter, since only the ratio between the two is on trial.

The hypothesis is supported by several observations. Morton (1946) has reviewed the evidence that painful breasts, so common a feature of the syndrome, are due to a high oestrogenic level, and he (Morton, 1950) was able to induce the syndrome artificially by the administration of large doses of oestrogens in two castrates and one post-menopausal woman, thus confirming the earlier observations of Singh *et al.* (1947). That the administration of progesterone is effective in relieving it was shown by Gray (1941), Puech (1942), and Albeaux-Fernet and Loublie (1946), and has been amply confirmed by ourselves. The hypothesis is further supported by the experimental evidence produced by Gillman (1942), who showed that progesterone administered to baboons reduces oestrogenic perineal swelling to normal in from four to seven days, an observation confirmed by Krohn (1951). Herlant (1939) had previously suggested that this effect was due to the suppression of the gonadotrophic activity of the pituitary by progesterone, but Krohn pointed out that the effects are too rapid for such an explanation and thought that a direct antagonism in this respect between oestrogens and progesterone was a more likely explanation. The pregnanediol output was subnormal in 10 of Morton's (1950) 29 patients, the endometrial pattern showed progestational deficiency in 22, and the basal temperature curve was "anovular" in 23.

Water Retention and the Oestradiol/Progesterone Ratio

If water retention due to an abnormally high oestradiol/progesterone ratio is the cause of the symptoms, how is it brought about? Several explanations have been postulated. Is there, for instance, a change in the metabolism of sodium, a sodium retention bringing about a water retention? Thorn, Nelson, and Thorn (1938) and Thorn and Emerson (1940) found that the excretion of sodium and chloride is decreased before and increased after both ovulation and menstruation. Morton (1950) found at these times a diminished excretion not only of sodium but also of potassium and chloride. Danforth *et al.* (1946) failed to find any consistent fluctuation in sodium or potassium metabolism, but confirmed the common rise in weight reported by other workers and found it to be associated with a decline in haematocrit and plasma proteins. Greisheimer *et al.* (1946) found no constant menstrual change in the blood, in *p*H, CO_2 content, chloride, or total base either in the premenstrual syndrome or in the controls, and concluded that the menstrual cycle is not characterized by any regular change in the acid-base equilibrium of the serum. Males showed as much fluctuation as females. The success of the treatment of the premenstrual syndrome by reduction in sodium intake has been noted above.

Many points are still obscure and several difficulties in interpretation have yet to be overcome; it does, however, appear that the best working hypothesis is that which postulates a cyclical change in sodium (and therefore in water) metabolism which occurs to a slight extent in healthy women and to an exaggerated extent in sufferers from the premenstrual syndrome. The rhythm of this change seems to be controlled by the level of oestradiol in the tissues, and this in its turn to be under the partial control of progesterone. Excessive water retention may therefore be present even with a fairly low level of oestradiol if progesterone is entirely lacking; or absent even with a very high level of oestradiol if progesterone is present in adequate amounts. It is the oestradiol/progesterone ratio which determines whether or not symptoms occur.

Symptomatology

If this hypothesis is correct a ready explanation of many of the symptoms is available.

Migraine and lesser degrees of headache may well be due to an increased hydration within the indistensible cranium. We have seen a male patient suffering from the oliguria and water retention which so often follow epidemic encephalitis who had frequent attacks of the severest migraine which were entirely prevented by the reduction of salt and water in his diet and the administration of urea. That urea is a useful treatment in some cases of migraine was always taught by Sir Walter Langdon-Brown and has been often confirmed by many workers—for example, Brown (1943)—and on other grounds water retention has been incriminated in migraine by the work of Földes (1933) and of Goldzieher (1941). Bickers and Woods (1951) produced the symptoms of the premenstrual syndrome by the injection of "pitressin" and found a close correlation between the consequent gain in weight, the severity of the symptoms, and the subsequent diuresis. The occasional epileptiform fits may be looked upon as the natural counterpart of the pitressin–water test for epilepsy.

There is no evidence that fluid retention causes bronchospasm. Indeed, the persistence over several days of premenstrual "asthma" suggests that the bronchial obstruction may be due to a less transient cause. A more prolonged obstruction by swelling of the mucosa may be present, though we have not yet confirmed this suggestion by bronchoscopy. The relationship between hyperaemia and oedema of the upper respiratory tract and the pelvic organs has long been recognized. It has been briefly reviewed by Greene (1943). The relationship was known to Hippocrates and was brought to the attention of the moderns by Mackenzie as early as 1884. He observed that the nasal mucosa of women becomes congested before the menstrual periods and that actual bleeding may then occur ("vicarious menstruation"). Some women, as Hoseason (1938) pointed out, suffer at this time from rhinorrhoea. Mortimer *et al.* (1936, 1937, 1939) showed that in monkeys there is an increase in colour of the nasal mucosa at monthly intervals coincident with the swelling of the sexual skin. The nasal changes were, indeed, 8% more regular as a sign of ovarian activity than menstrual bleeding itself, and were most obvious in the fertile months of September and October. Immature and adult monkeys of both sexes, whether intact or castrate, react to oestrogenic treatment by reddening of the nasal mucosa, which occurs even if the nasal tissue is transplanted elsewhere (Bachman *et al.*, 1936).

The papers from the Montreal school were followed by several clinical reports of good results in the treatment of atrophic rhinitis by injections or local applications of oestrogenic substances. That these results may be accounted for by the selective concentration of oestrogens in the nose is suggested by the experiments of Fisher *et al.* (1936). The immediate effect of this concentration is local vasodilatation, as Reynolds and Foster (1940) showed. Apart from their specific action, oestrogens produce hyperaemia in many tissues (Hechter *et al.*, 1940) and it is natural that this hyperaemia should be greatest in those tissues in which a concentration of oestrogens occurs. This hyperaemia is due to the liberation of acetylcholine in these situations (Reynolds, 1939; Reynolds and Foster, 1940), and effects similar to those of oestrogens may indeed be obtained by spraying the nose with neostigmine (Bernheimer and Soskin, 1940). The rhinorrhoea of the premenstrual syndrome—and perhaps the asthma as well—is thus explicable by the excessive local activity of oestradiol which would be expected *ex hypothesi*. The oedematous nasal mucosa may lead to blocking of the exits from the nasal sinuses and consequent "vacuum headaches."

The occasional association of premenstrual mastodynia with the commoner symptoms can be plausibly explained by the relatively high oestrogenic level without involving the consequent water retention. The evidence that the "painful nodular breast" is caused by excessive oestrogenic stimulation has been reviewed by Morton (1946) and by Greene (1950).

That so-called rheumatic pains may be due to water retention is well recognized. The rather ill-defined pain and tenderness in the soft tissues of obese women (often referred

to as "fibrositis" and "panniculitis") usually responds well to a dehydrating regime. A possible explanation has been offered by Copeman (1949).

The dermatoses of the premenstrual syndrome are less readily explicable on the present hypothesis. The explanation must await further work on the relationship between steroid metabolism and the state of the human skin. That such a relationship exists is clinically obvious. The laboratory evidence has been reviewed by Burrows (1945).

Treatment of the Syndrome

It has been indicated that numerous treatments have been suggested in the past. These include the following.

Dehydration.—References to this method of treatment have been cited in the discussion on the possibility that water retention is the cause of the syndrome. There seems little doubt that in a fair proportion of cases it is effective. It was not adopted in the present series. It has been tried by one of us (R. G.) in earlier cases with occasional success. It is greatly disliked by the patients, and only those suffering from the severest symptoms can be bothered with it for more than a few months. The newer diuretics have not been tried.

Androgens.—The "literature" of the subject leaves little doubt that androgens may be useful (Greenblatt, 1940; Albeaux-Fernet and Loublie, 1946; Freed, 1945, 1946; Chiray *et al.*, 1940). Androgens, such as testosterone propionate, which must be administered by injection, are no longer worthy of serious consideration. Methyltestosterone, administered by mouth, is sometimes effective, especially in those patients in whom mastalgia is a prominent symptom. It is less generally successful than progesterone in relieving other symptoms of the syndrome. Its chief disadvantage is the danger of virilization. It occasionally happens that the dose needed to relieve symptoms is high enough to cause acne, the growth of a slight moustache, and lowering of the voice. Menstruation may be suppressed.

Vitamins.—M. S. Biskind (1943) was influenced in his views by the occurrence of glossitis in the syndrome and obtained relief by the administration of vitamin B. He quoted G. R. Biskind and Mark (1939), who had shown that in vitamin-B deficiency the liver's ability to inactivate oestrogens may be impaired. With G. R. Biskind and L. H. Biskind (1944) he published 11 cases, all relieved by this therapy. In a small series treated by one of us (R. G.) before the present one was begun no success was achieved. Bickers and Woods (1951) were also unsuccessful. The effectiveness of vitamin A has been vouched for by Argonz and Abinzano (1950). Vitamin A has not been tried by us. If, as is suggested, its efficacy depends on its diuretic properties, it can hardly be expected to compete with mersalyl, urea, or the newer diuretic drugs.

Oophorectomy and X-ray Treatment of Ovaries.—These have been used successfully by Frank (1931). They are measures obviously too drastic for the present day.

Treatment with Progestogens

Progesterone has been used successfully by Gray (1941), Puech (1942), and Albeaux-Fernet and Loublie (1946). These workers administered the hormone by intramuscular injection. No report has so far appeared of the use of ethisterone, or of progesterone other than by intramuscular injection.

All patients in this series were treated by means of progestogens. The results of the treatment of 84 patients are presented. All were treated between January, 1948, and June, 1952, some of those included in the analysis of symptoms being excluded from consideration here for lack of a sufficiently long period of observation.

Cases of mild and moderate severity were treated at first by means of ethisterone, given in oral doses of 30 to 150 mg. daily for twelve days from the fourteenth day of the cycle. If at the end of the cycle a patient remained symptom-free, she was observed at monthly intervals. If she improved without becoming symptom-free, treatment was continued

TABLE X.—*Results of Treatment*

No.	Symptoms	Ethisterone	Progesterone	Final Treatment	Side-effects
1	Asthma	—	Free	Implant 10.52	—
2	Migraine	No relief	,,	,, 10.52	—
3	,,	—	,,	Observation 3/12	Dysmenorrhoea
4	,,	Improved	,,	Implant 10.52	—
5	,,	—	,,	,, 6.51	—
7	,,	Free	—	Observation 4/12	—
8	Oedema	,,	—	Implant 10.49	Heavy periods with clots
9	Acne	Improved	—	Observation 4/12	Dysmenorrhoea
10	Rheumatism	—	Free	Implant 11.52	—
11	Acrocyanosis	Improved	Improved	,, 10.52	—
12	Migraine	Free	Free	,, 4.51	—
13	,,	—	,,	,, 2.52	Amenorrhoea 8/52
14	,,	No relief	,,	,, 6.48	—
15	Asthma	—	,,	,, 1-49	—
16	Migraine	—	,,	Observation 7/12	Erythema at injection site
17	,,	—	,,	Implant 2.50	Shorter cycle, heavier loss
22	,,	—	,,	,, 2.49	Hyperchromic anaemia. Hb 49%
23	Vertigo	—	,,	Observation 5/12	—
24	Styes	Free	,,	,, 5/12	Nausea with each injection
25	Migraine	,,	—	,, 3/12	—
26	,,	,,	Free	,, 3½ years	—
27	Acne	Improved	Improved	,, 3/12	—
28	Asthma	—	Free	Implant 12.48	—
29	Migraine	Free	,,	Observation 2/12	—
31	Rheumatism	—	,,	,, 4/12	—
32	,,	—	,,	Implant 11.49	—
33	Migraine	Postponed attack	,,	Observation 3/12	—
34	,,	No relief	Not known	Did not return	—
35	Petit mal	Free	—	Ethisterone	—
36	Migraine	,,	Free	Implant 2.51	—
37	Petit mal	No relief	No relief	Improved on testosterone	—
38	Migraine	Free	Free	Implant 7.52	—
39	,,	—	,,	,, 6.50	—
40	,,	—	,,	Observation 6/12	—
41	Rheumatism	—	,,	,, 10/12	—
42	Migraine	No relief	,,	Implant 11.51	—
43	,,	Free	—	,, 7.52	—
44	Erythema multiforme	No relief	Free	Progesterone injections	—
45	Migraine	—	,,	Observation 7/12	—
46	,,	—	,,	,, 14/12	—
47	Migraine and seborrhoeic dermatitis	Improved	,,	,, 7/12	Erythema at injection site
48	Migraine	—	,,	Implant 4.52	—
49	,,	—	,,	Observation 5/12	—
50	Asthma	—	,,	Implant 9.52	—
51	Eczema	—	Improved	Observation 5/12	—
52	Irritability	—	Free	Implant 12.48	—
53	Migraine	No relief	No relief	Free on testosterone	—
54	Acne	Improved	—	Observation 4/12	—
55	Migraine	No relief	Free	Progesterone injections	Sl. ovulatory bleeding
56	,,	,, ,,	Not known	Did not return	—
57	,,	Improved	Free	Observation 5/12	—
58	Glossitis	Free	—	,, 3 years	—
59	Glossitis and petit mal	,,	—	,, 3 ,,	
60	Migraine	—	Free	,, 8/12	—
61	Nausea	—	,,	Implant 2.49	—
62	Migraine	Free	—	Continuing ethisterone	—
63	,,	,,	—	Observation 5/12	Longer period
64	,,	,,	—	,, 5/12	—
65	Rheumatism	—	Free	,, 3/12	—
67	Migraine	—	,,	,, 3/12	Erythema at injection site
68	,,	Free	—	,, 3/12	—
69	,,	Not known	No relief	No report after ethisterone	Headache with each injection
70	,,	No relief	Free	Awaiting implant	—
71	Irritability	Free	,,	Continuing ethisterone	—
72	Rheumatism	—	,,	Observation 3/12	—
73	Migraine	—	,,	Implant 11.52	—
74	,,	No relief	,,	Observation 2/12	—
75	,,	Free	—	,, 5/12	—
76	,,	,,	—	Continuing ethisterone	—
77	,,	No relief	Improved	Progesterone injections	Sl. ovulatory bleeding
78	,,	Free	—	Continuing ethisterone	—
79	,,	Improved	Free	,, ,,	—

TABLE X.—*(Continued)*

No.	Symptoms	Ethisterone	Progesterone	Final Treatment	Side-effects
80	Rheumatism	—	Free	Observation 2½ years	—
81	Nausea	—	,,	Observation 2½ years	—
82	Migraine	—	No relief	Artificial menopause; migraine now worse	—
84	,,	Free	—	Continuing ethisterone	—
85	Styes	No relief	Free	Awaiting implant	—
86	Migraine	,, ,,	,,	Implant 10.52	—

Cases 6, 18, 19, 20, 21, 30, 66, and 83 did not report back after treatment.
Cases 85 and 86 not included in previous analysis owing to insufficient history.

until she became symptom-free. If no improvement occurred she was given intramuscular injections of progesterone instead, in doses at first of 10 mg. daily during the second half of the cycle. Later it was found that an injection of 25 mg. on alternate days was equally effective. Severe cases were treated by this method from the outset. Patients who responded to this treatment were kept under observation: if they were only improved, treatment was continued until they were symptom-free. Those who became symptom-free but afterwards relapsed for lack of treatment were selected for treatment by means of implantation, doses from 200 to 500 mg. being employed. In a few cases in which treatment with oral ethisterone or intramuscular progesterone was used, the symptoms instead of being completely relieved were postponed until the later days of menstruation or even until the post-menstrual phase. Such patients were subsequently treated with ethisterone or progesterone throughout the entire month, and were ultimately treated by implantation.

Tables X and XI show the results obtained. The oral administration of ethisterone gave complete relief in 22 cases (47.9%) and partial relief in a further 8 cases (17.4%).

TABLE XI.—*Comparison of Results of Treatment with Ethisterone and Progesterone Injections*

Result	Ethisterone		Progesterone		Total After Final Treatment	
	No.	%	No.	%	No.	%
Symptom-free ..	22	47·9	51	83·5	66	84·7
Improved ..	8	17·4	4	6·6	6	7·7
Postponed attack	1	2·1	—	—	—	—
No relief ..	14	30·5	4	6·6	3	3·8
Not known ..	1	2·1	2	3·3	3	3·8
Total ..	46	100	61	100	78	100

Of the 14 cases unsuccessfully treated 9 had complete relief and 1 partial relief when treated with intramuscular progesterone, 2 obtained no relief from intramuscular progesterone, and 2 patients did not report the result. The results with intramuscular progesterone in 61 cases were more satisfactory—51 (83.5%) became free from symptoms, 4 (6.6%) improved, and 4 (6.6%) obtained no relief. Of the 4 patients unsuccessfully treated with progesterone 2 were treated with methyltestosterone, 5 mg. twice daily, from which one obtained complete relief and one partial relief. One patient unsuccessfully treated failed to report the result of treatment with ethisterone. The remaining unsuccessfully treated woman, aged 45, had suffered from toxaemia in all her five pregnancies and had been sterilized in 1942. In 1949, after the unsuccessful trial of progesterone, she was given an artificial menopause by means of radiotherapy. After this her migraine, which had previously been premenstrual, became weekly, and had remained so when last seen in March, 1952.

Table XII summarizes the final treatment of 78 patients: thirty are symptom-free without regular medication and 4 so much improved that regular medication is unnecessary; 28 were treated with progesterone implants, and, of these, 27 had complete relief and one partial relief of symptoms.

TABLE XII.—*Final Treatment in 78 Cases*

Final Treatment	Total Cases	Total %	Free		Improved		No Relief
			No.	%	No.	%	
Observation	34	43·6	30	44·7	4	57·1	—
Progesterone implant ..	28	35·8	27	40·5	1	14·3	—
Continuing ethisterone	7	8·9	7	10·4	—	—	—
,, progesterone	3	3·9	2	2·9	1	14·3	—
Testosterone	2	2·6	1	1·5	1	14·3	—
Artificial menopause ..	1	1·3	—	—	—	—	1*
Not completed	3	3·9					
	78	100	67	100	7	100	1

In three cases "not completed," patients did not report after change of treatment.
* Migraine worse after artificial menopause.

Summary

A large proportion of women, estimated by one author as 40%, suffer a variety of distressing symptoms during the final week or so of the menstrual cycle. In occasional cases, similar symptoms may occur at monthly intervals at other points of the cycle. They are probably produced by water-retention, and the evidence at present available suggests that this in its turn is due to abnormal elevation of the oestradiol/progesterone ratio.

Various treatments aimed at either dehydration or a correction of the disturbed hormonal ratio have proved partially effective. Treatment with a progestogen is almost invariably successful. In mild cases relief is usually obtained by the oral administration of ethisterone in a dosage of 25 mg. twice daily during the second half of the menstrual cycle. A larger proportion of patients can be relieved by the intramuscular injection of progesterone, 25 mg. on alternate days during the same phase of the cycle. Such cases are more effectively treated, with less labour for the patient, by the implantation of progesterone, which remains effective for many months.

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THE PREMENSTRUAL TENSION SYNDROME AND ITS TREATMENT

BY

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Premenstrual tension is a syndrome occurring during the second half of the menstrual cycle and consisting of a number of mental and physical symptoms. The syndrome is composed of marked general tension and irritability, together with one or more of the following symptoms: anxiety, depression, bloated abdominal feelings, swelling of subcutaneous tissues, nausea, fatigue, painful swelling of the breasts, headaches, dizziness, and palpitations. Less frequently there may be increased sex desire, excessive thirst, increased appetite, and hypersomnia. The symptoms usually start about seven to fourteen days before menstruation and pass off soon after the onset of the menses, although some patients continue to have symptoms throughout the period. The syndrome must not be confused with the premenstrual discomfort experienced by many women. The premenstrual tension syndrome may seriously interfere with work and social activities, and can be incapacitating. The condition is by no means as uncommon as suggested in some reports.

Literature

The aetiology of the condition is still obscure. Frank (1931), who introduced the term "premenstrual tension," considered it to be due to excess of circulating oestrogen. Israel (1938) believed the syndrome not to be due to excess oestrogen itself, but rather to the action of unantagonized oestrogen resulting from faulty luteinization. Gillman (1942) and Hamblen (1945), in contrast, implicate progesterone as the responsible hormone. Convincing evidence in support of the hypothesis of faulty luteinization permitting the action of unantagonized oestrogen as the primary cause of premenstrual tension is, however, given by Morton (1950).

Water retention is postulated by Greenhill and Freed (1941) as the immediate cause of premenstrual tension symptoms. Hoffman (1944) considered that an unstable nervous system was an important factor, and a number of authors have expressed the opinion that the condition seems to be more frequent in unstable women.

Rees (1953), in a psychosomatic study of 145 subjects, including normal and psychiatric patients, found that marked premenstrual tension could exist in normal women of stable personality and that many severely neurotic women were free from it. In neurotic patients with premenstrual tension there was a positive correlation between degree of premenstrual tension and degree of personality instability and severity of neurosis. Rees, while in general supporting the theory that the condition was primarily physiogenic and due to changes resulting from defective progesterone secretion, stressed that the syndrome was of complex causation in which personality and constitutional and emotional factors operate in addition to the primary physiogenic changes.

There is now considerable evidence to suggest that the bodily changes of the premenstrual tension syndrome are primarily due to a lack of progesterone, which allows the unopposed action of oestrogens during the second half of the menstrual cycle. It is known that oestrogens cause sodium and water retention. Hydration is a common feature of the premenstrual tension state, and many patients put on from 2 to 9 lb. (0.45 to 4.1 kg.) in weight during the premenstrual phase and lose a corresponding amount with the diuresis following the onset of the menses. Oestrogens stimulate growth of the epithelia of the breast, vagina, and endometrium, and this together with hydration may account for painful swelling of the breasts. Hypoglycaemia and hyperinsulism have been noted to occur during premenstrual tension states (Billig and Spaulding, 1947; Morton, 1950) and may be the cause of increased appetite and fatigue noted in some patients. These changes in the internal environment cause a number of specific symptoms and also may result in autonomic lability, causing such symptoms as palpitations and dizziness. The patient's reaction to these changes can be influenced by such factors as personality type and stability, emotions, attitudes, and degree of autonomic instability.

The treatment of premenstrual tension can therefore be directed at different aetiological levels. (1) Psychotherapy, including explanation and re-education to improve attitudes, relieve symptoms, and minimize degree of incapacity. (2) Dehydration by means of diuretics to relieve symptoms due to hydration and possibly to facilitate elimination of the noxic agent. (3) Administration of progestogens to compensate for any lack of progesterone and to antagonize action of oestrogens. (4) Administration of androgens to antagonize action of oestrogens as suggested by Greenblatt (1940), Geist (1941), and Freed (1945).

Gonadotrophins are generally considered to be ineffective (Bowes, 1950), and as oestrogens tend to intensify symptoms (Morton, 1950) they are contraindicated.

Present Investigation

The following therapeutic methods have been studied in a group of 30 patients suffering from severe premenstrual tension: psychotherapy; dehydration therapy using ammonium chloride; administration of progestogens, including progesterone by injection and ethisterone by mouth; and administration of androgens in the form of methyltestosterone by mouth. The patients have been observed for from six months to four years, giving a total of 207 cycles.

The assessment of premenstrual tension was made from data obtained during clinical interview and from special daily records of symptoms. Detailed instructions were given to patients regarding the daily recording of symptoms, so that scoring was, so far as possible, kept standardized. The day-to-day records were kept for some months before starting treatment, and the data so provided permitted a detailed assessment of the premenstrual tension and provided a baseline for measuring the effects of treatment.

Clinical Data.—The age distribution of the group was 15–24 years, 8%; 25–34, 56%; 35–44, 36%. Most patients had developed premenstrual tension before 35 and about one-fifth before the age of 20. Two developed premenstrual tension after childbirth, and three just before the menopause. 80% of the group were married. The mean age of menarche was 14.7 years and the frequency distribution of menarchial ages was similar to that described by Ellis (1947) for normal British women. The symptoms of premenstrual

tension usually started about seven to ten days before the period and usually cleared up soon after the onset of menstrual flow, but in some patients they occasionally continued throughout the menses. The symptomatology of the group was as follows: tension, 100% ; irritability, 100% ; depression, 80% ; emotional lability, 80% ; anxiety, 73% ; swelling of fingers or legs, 73% ; painful swelling of breasts, 63% ; fatigue, 63% ; headaches, 63% ; insomnia, 40% ; pruritus, 40% ; palpitations, 40% ; nausea, 37% ; marked thirst, 20%.

Results

Psychotherapy

Premenstrual tension was not found to be amenable to psychotherapy alone. Psychotherapy of a simple kind can help the patient in understanding the condition and can improve her attitude and reaction to it. The tense, anxious, striving obsessional type of woman feels greatly frustrated by the interference with physical, mental, and social well-being caused by the premenstrual tension state. She may tend to force herself to keep up the tempo of her work and life in spite of her symptoms. This tends to lead to greater frustration and increase in tension. In this type of patient an understanding of the nature of the condition and the fact that there is an underlying physiological basis for her symptoms can help, together with the advice to modify the demands she makes on herself in relation to her premenstrual symptoms. The person who, on the other hand, is hypochondriacal or very dependent may allow the premenstrual tension state to interfere unnecessarily with her work and social activities. Again explanation, and re-education with the aim of producing a more salutary attitude to her symptoms, can be helpful.

Sixteen patients of the group were attending the psychiatric clinic for treatment of neurosis in addition to premenstrual symptoms. In all these the onset of premenstrual tension antedated the onset of neurosis. Some of them recovered from their neurosis without any significant improvement in premenstrual tension symptoms; conversely, some patients showed improvement in premenstrual tension with hormonal therapy without change in the coexisting neurosis. These facts indicate that premenstrual tension cannot be regarded as being primarily a neurosis.

Suggestion is not thought to play an important part in the condition. Most of the patients develop premenstrual symptoms without realizing the relationship to the menstrual cycle. Exhibition of inert tablets given as a control to hormone therapy produced no significant improvement.

Dehydration Therapy

Dehydration treatment was applied by giving enteric-coated tablets of ammonium chloride in 7½–15-gr. (0.5–1-g.) doses three times a day for twelve days before the period, with restriction of sodium intake. This was found to be effective in preventing the development of swelling of the fingers, legs, face, and other parts of the body. It was also successful in removing these if they had already developed.

The majority of patients reported that they felt more comfortable and had relief of the following symptoms in particular: bloated feeling in abdomen, heavy feelings in head, swelling of subcutaneous tissues and tightness of skin, general pruritus, and pruritus vulvae.

Although effective in preventing excessive water retention and its attendant symptoms, the method was not always effective in relieving the nervous tension, irritability, depression, and anxiety. This suggests that hydration is not responsible for all the symptoms of the syndrome. This is borne out, too, by the fact that some women develop signs of hydration midway between the periods without the emotional tension that develops premenstrually, and in some patients the nervous tension disappears at the onset of the menses in spite of the fact that hydration may continue for some days afterwards.

Progesterone Treatment

Progesterone was given intramuscularly on alternate days for twelve days before the period in five patients, and was found to be effective in relieving the symptoms of premenstrual tension. In view of the practical disadvantage of a treatment involving a series of injections an extensive trial was given to the orally active preparation ethisterone. This was given to all patients in the series, and observations were made on over 100 cycles.

Ethisterone was given for twelve days before the period, starting with 5 mg. twice daily, increasing to 10 mg. twice daily if necessary. Most patients responded to a dosage of 5–10 mg. daily. In about 85% of the trials ethisterone was found to produce significant relief of premenstrual symptoms. The signs and symptoms of hydration were prevented and there was usually relief of tension, anxiety, depression, fatigue, headaches, bloated feelings, and pruritus. The pain of dysmenorrhoea was not relieved, and often the patient reported increased pain indicative of more powerful uterine contractions. Occasionally delay of a few days in the onset of the menses was noted when the patient was on ethisterone.

Androgen Treatment

Treatment with methyltestosterone has been tried in 10 patients and observations were made on 40 cycles. It was given in doses of 10 mg. daily for twelve days before the period. Marked relief of premenstrual tension symptoms was obtained, including tension, irritability, anxiety, and depression; also signs and symptoms relating to hydration were prevented. As with ethisterone, the period may be delayed and uterine contractions more painful.

The relief of symptoms of premenstrual tension with methyltestosterone seems to be as effective as that given by ethisterone.

Discussion

The complex symptomatology comprising the premenstrual tension syndrome is of multiple causation. Some of the symptoms and signs are attributable to the effects of hydration, others are due to proliferative changes in the breasts and uterus. Some are possibly due to changes in blood sugar, whereas others are manifestations of autonomic imbalance. Subjective factors, such as the patient's emotional stability, personality, and her attitudes, will also influence the intensity of the degree of incapacity resulting from various symptoms.

Our observations and therapeutic results appear to lend support to the theory that the primary cause is lack of progesterone secretion, permitting the unantagonized action of oestrogens.

Oestrogens are known to cause sodium ion and water retention and proliferative changes in the breast and endometrium, and also to cause various chemical changes in the blood, including hypoglycaemia and increased carbohydrate tolerance (Billig and Spalding, 1947 ; Morton, 1950). These effects would appear to explain many of the symptoms and changes associated with the premenstrual tension state.

Treatment with ammonium chloride causes diuresis and removes or prevents excessive hydration, and may also serve to aid the excretion of oestrogens or other agents that may be pathogenetic in premenstrual tension. Our evidence suggests, however, that hydration does not account for the whole of the syndrome.

Progesterone and ethisterone treatment was found to be effective in alleviating not only hydration and its symptoms but also nervous tension, irritability, depression, anxiety, etc. Progesterone promotes diuresis (Selye, 1950), and our observations with ethisterone suggest a similar effect, in contrast to the water-retaining effects of oestrogens. Testosterone also promotes diuresis (Selye, 1950) and is similar in chemical constitution to ethisterone.

Ethisterone and testosterone are both diuretic and antagonistic to oestrogen, and this would appear to be the rationale for their beneficial therapeutic effects on premenstrual tension.

The conclusion is that the simplest method of treating premenstrual tension is by means of diuretics such as ammonium chloride, and, if this is not effective, ethisterone or methyltestosterone should be tried.

Summary

The clinical features of premenstrual tension are described and the possible mode of origin of the various symptoms is discussed. Hydration, blood chemistry changes, autonomic nervous system responses, as well as psychogenic and personality factors are believed to play a part in the syndrome. A working hypothesis on which treatment was based is postulated.

Treatment was applied at various aetiological levels, including psychotherapy, dehydration therapy, and administration of progestogens and androgens.

Psychotherapy has an important but limited role. Dehydration therapy was found to alleviate some of the symptoms only. The most effective methods of treatment were administration of a progestogen such as ethisterone or an androgen such as methyltestosterone during the second half of the menstrual cycle.

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BRIGHT'S DISEASE

AN ATTEMPT AT A STATISTICAL ASSESSMENT OF THE CLASSIFICATION PROPOSED BY ELLIS

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[WITH SPECIAL PLATE]

In 1827 Richard Bright described the disease of the kidney to which his name is still attached. His cases included all forms of renal disease unassociated with obvious changes in the lower urinary tract, and so were composed mainly of the three main groups of chronic pyelonephritis, hypertensive nephrosclerosis, and true nephritis. The second of these was clearly separated by Allbutt (1895–6), and the last has been defined by Osler (quoted by Osman, 1939) as "bilateral, non-suppurative inflammatory disease of the kidneys." The importance and frequency of the first group as a cause of Bright's disease has only recently been recognized.

Numerous attempts have been made to subdivide these cases, but none has received general acceptance. Ellis (1942), as a result of a combined clinical and pathological investigation of "about 600" cases, "about 200" of which were fatal, suggested that nephritis could well be separated into only two groups, which he called types I and II.

Type I nephritis is characterized by an abrupt onset with haematuria, and is often preceded by an acute infection such as a sore throat. In most adequately treated cases recovery is complete. Death may occur in the acute stage, and some cases follow a progressive course ending in death in a few months. Other cases appear to recover completely, yet after many years develop renal failure and hypertension.

Type II nephritis, on the other hand, is of insidious onset and usually presents as oedema with albuminuria. There is no history of preceding infection, and haematuria is uncommon. The course of the disease is steadily downhill, and if renal failure and hypertension supervene the oedema tends to abate. Many of these patients die from secondary infection and the remainder from hypertension or uraemia.

Ellis further suggested that the two types were not only clinically distinct but were associated with specific renal histological changes and were unrelated aetiologically. Davson and Platt (1949) supported his conclusions with the exception of the last, upon which they reserved judgment.

The present communication describes a similar investigation of a comparable group of cases, with the difference that, where possible, clinical and pathological diagnoses were made quite independently. There were two main objects. The first was to examine the lesions found in fatal Bright's disease, and the second was to see what support analysis of a further group of cases lent to Ellis's views.

Material and Method

In all, 154 cases were examined. They were those that had been indexed as Bright's disease in the necropsy records of this hospital during 1931–51. No non-fatal cases were investigated, so no comprehensive survey of the natural history of these diseases can be offered.

Twenty-seven of these cases have not been included in the analyses: 8 of them because there was a history of toxaemia of pregnancy, 2 because of industrial exposure to heavy metals; 1 was a typical case of polyarteritis nodosa, and 1 was associated with scleroderma; in the remaining 15 cases the clinical or pathological material was incomplete.

The clinical diagnoses were made on the ward records, which were examined by C. L. J., only very few of the patients being seen by either of us during life. The original necropsy reports were consulted, where necessary, only for the macroscopic observations, the histological data presented being derived from an examination of preserved material by J. B. E. At first these investigations were entirely independent, and extreme care has been exercised to avoid either diagnosis being influenced by evidence proper to the other. In all cases in which clinical and pathological diagnoses differed a re-examination was made, the only additional information at each observer's disposal then being the fact that a discrepancy had been encountered. It was rarely found possible to alter a diagnosis at this stage, and if agreement was not reached the available information was discussed and a definite decision on grouping was made. In only 9 cases (7.1%) was agreement then reached, leaving 19 cases of disagreement. All analyses, except where otherwise stated, have been based on the assumption that, wherever pathological and clinical conclusions conflicted, those drawn from the latter material were the correct ones.

Nomenclature

The classification proposed by Ellis has been used throughout, and his criteria for the diagnosis of nephritis of

types I and II have been strictly adhered to. He does not include chronic interstitial nephritis in his table, but follows the recent trend of referring to these cases as chronic pyelonephritis (Ellis and Evans, 1933; Longcope and Winkenwerder, 1933; Weiss and Parker, 1939; Platt and Davson, 1950), of which condition they are thought to represent a healing or healed stage. In our diagnoses we have depended largely on the descriptions quoted, and since the lesions closely resemble those of the healing stage of "ascending" renal infection we shall, for convenience, call them "chronic pyelonephritis."

The term "nephrosis" is restricted to a predominantly tubular condition in which there is no evidence whatever of inflammatory disease and of which we have encountered only one case.

In the diagnosis of nephrosclerosis the descriptions of Allbutt (1895–6), Ellis (1938), and Platt (1948) have been followed.

The other conditions in Ellis's table have been seen in numbers too small to merit further discussion (e.g., amyloidosis), or not at all (e.g., focal nephritis), or have been excluded (e.g., toxaemia of pregnancy).

Results

Of the 154 cases examined 15 had been admitted in terminal uraemia, and, although clear histological pictures were seen in 13 of them, no further clinical diagnosis could be made. In the remaining two of these and in seven other cases in which the diagnosis could be established clinically, no more precise conclusion than "contracted kidney" (see below) could be reached from the pathological material. In 16 cases renal lesions were unexpected necropsy findings to which there were no relevant clinical notes. In the remaining 116 cases clinical and pathological diagnoses could be made.

TABLE I.—*Distribution of the Cases by Their Clinical Diagnoses*

	This Series	Platt and Davson (1950)*
Acute type I nephritis	9	23
Chronic type I nephritis	21	
Type II nephritis	24	25
Pyelonephritis	12	26
Benign nephrosclerosis	14	16
Malignant hypertension (primary)	13	24
Amyloid disease	2	3
Lipoid nephrosis	1	
Clinical uraemia (Table IIIA)	15	
Incidental necropsy findings of Bright's disease (Table IIIB)	16	
	127	
Toxaemia of pregnancy	8	2
Exposure to heavy metals	2	
Scleroderma	1	1
Polyarteritis nodosa	1	15
No diagnosis	15	
	154	

* These authors made their diagnoses on all available clinical and pathological information; in our series this procedure would have doubled the number of cases of pyelonephritis.

From Table I it will be seen that the distribution of the cases in the major groups is roughly the same as that found in the similar table of Platt and Davson (1950), but the ratio of type I to type II cases is higher than in the fatal cases of Ellis's (1942) series.

Table II shows those 89 cases in which a definite diagnosis of a specific condition could be made on both clinical and pathological grounds, together with the agreements between these diagnoses. In this analysis the number of cases in which agreement has been reached is also expressed as a percentage of the number of clinical and of pathological diagnoses alone and in combination (lines 2, 3, and 4). The total number of cases in line 4 is greater than that in lines 2 and 3 by the 19 cases in which agreement was not reached, for these appear in it twice.

The degree of accuracy of the clinical and pathological diagnoses individually considered is somewhat variable among the different conditions. The lowest figures are seen for the clinical and combined diagnoses of chronic type I nephritis, but only the latter differ significantly from the accuracy of diagnosis of the rest of the inflammatory group (difference 26%, standard error (s.e.) ± 14%; difference 30%, s.e. ± 13%). Significantly greater accuracy was achieved in both clinical and pathological diagnoses of degenerative as opposed to inflammatory disease (differences 21%, s.e. ± 8%), for the clinical diagnosis of chronic pyelonephritis (difference 35%, s.e. ± 7%), and for the pathological diagnosis of acute type I nephritis (difference 32%, s.e. ± 6%). All other differences may have arisen by chance. In the group of cases in which the clinical or pathological diagnosis was chronic type I or type II nephritis agreement was reached in less than two-thirds of them (63%).

Significant agreements between the clinical and pathological diagnoses combined are seen in all the large groups, but they are not all of the same order. Thus those for degenerative disease (93%, s.e. ± 4.7%, = 20 × s.e.) and for acute type of I nephritis (78%, s.e. ± 12%, = 6 × s.e.) are better than those for the chronic inflammatory conditions (47–57%, approximately 5 × s.e.), all three of which are closely similar.

In the first two groups in Table III renal disease was unsuspected until it became manifest at routine necropsy or by the onset of uraemia. About half of the recognizable cases in these groups—that is, excluding the two cases of contracted kidneys—are chronic pyelonephritis (52%), a significantly higher incidence than in the whole series (difference 23%, s.e. ± 10%). The remainder of the cases are distributed among the other forms of renal disease in proportions similar to those shown in Table II (3).

In the remaining group the pathological findings were widespread extreme glomerular hyalinization with interstitial fibrosis and arteriolar hypertrophy. They probably represent patients with two or more pathological processes, such as chronic pyelonephritis superimposed upon chronic type I nephritis, with the subsequent addition of benign hypertensive sclerosis. No definite diagnosis was made, and they are referred to as contracted kidneys.

TABLE II.—*Cases Which Were Both Clinically and Pathologically Diagnosed as Specific Conditions*

	Acute Type I Nephritis	Chronic Type I Nephritis	Type II Nephritis	Chronic Pyelonephritis	Acute Microscopical Form of Periarteritis Nodosa	Total No. of Cases of Inflammatory Disease	Benign Nephrosclerosis	Primary Malignant Hypertension	Amyloid Disease	Lipoid Nephrosis	Total No. of Cases of Degenerative Disease	Combined Totals
(1) Diagnosis agreed	7	9	16	11	0	43	12	12	2	1	27	70
(2) Diagnosed clinically	9	17	23	11	0	60	13	13	2	1	29	89
% (1/2)	78	53	70	100	—	72	92	92	100	100	93	81
(3) Diagnosed pathologically	7	11	21	20	1	60	14	12	2	1	29	89
% (1/3)	100	82	26	55	0	72	86	100	100	100	93	81
(4) Diagnosed either clinically or pathologically	9	19	28	20	1	61	15	13	2	1	30	89
% (1/4)	78	47	57	55	0	70	80	92	100	100	93	81

TABLE III

A. *Histological Findings in Cases Clinically Diagnosed as Uraemia*

Chronic type I nephritis	2
Type II nephritis	2
Chronic pyelonephritis	7
Benign nephrosclerosis	1
Contracted kidneys	2
Kimmelstiel–Wilson lesions	1

B. *Forms of Bright's Disease Discovered Incidentally at Necropsy*

Acute type I nephritis	2
Chronic type I nephritis	1
Type II nephritis	5
Chronic pyelonephritis	8

C. *Clinical Diagnoses in Cases with "Contracted Kidneys"*

Chronic type I nephritis	4
Type II nephritis	1
Chronic pyelonephritis	1
Benign nephrosclerosis	1
Uraemia	2

Table IV gives the details of the discrepancies between clinical and pathological diagnoses of types I and II of nephritis. An illustrative case history for each important line of this table is given below, each being illustrated by a photomicrograph of a typical lesion (Cases 1–7; Plate, Figs. 1–7).

TABLE IV.—*Cases in Which a Diagnosis of Either Type I or Type II Nephritis was Made Either Clinically or Pathologically and in Which Agreement was Not Reached*

Case No. in Appendix	Clinical Diagnosis	Pathological Diagnosis	No. of Cases
1	Acute type I nephritis	Type II nephritis	1
		Polyarteritis nodosa	1
2	Chronic type I nephritis	Type II nephritis	4
3	" " "	Chronic pyelonephritis	3
4	" " "	Benign nephrosclerosis	1
5	Type II nephritis (probable)	Chronic type I nephritis	2
	" " " "	" pyelonephritis	3
6	" " " (definite)	" "	2
7	Benign nephrosclerosis	Type II nephritis	1
	Total		18

There were 11 cases in this series diagnosed clinically or pathologically as acute nephritis of type I. Nine of these were diagnosed pathologically as acute type I nephritis, and one, which was of about 14 days' duration, as early type II nephritis (Case 1). The acute microscopical form of polyarteritis nodosa (Davson *et al.*, 1948) was seen only once, but it was noted that acute inflammatory arterial lesions are not uncommon in diseased kidneys. They were seen in three cases in the present series (2%); in one diagnosed pathologically as type II nephritis and clinically as type I, in one of primary malignant hypertension, and in one in which that condition was due to chronic pyelonephritis. The diagnosis of polyarteritis was, however, made only when there was adequate supporting clinical and pathological evidence. Thus, while it seems possible that there is some relationship between nephritis and polyarteritis nodosa, as suggested by Davson *et al.* (1948), our cases are more in keeping with the classical view that acute glomerulonephritis is a clinico-pathological entity that may be fatal in the acute phase.

Case Reports

Case 1.—A woman aged 38 was admitted complaining of swelling of the legs for two days. One month previously she had had tonsillitis and had been sent to bed and given sulphonamides, with much improvement. Two weeks before admission she had a second attack, with slightly swollen ankles. This persisted and became much worse two days before admission. On examination her temperature was 102° F. (38.9° C.) and there was facial and ankle oedema. The blood pressure was 150/80 mm. Hg, and there were some tender enlarged lymph nodes in the anterior triangles of the neck. The urine was much reduced in amount and was of normal specific gravity. It contained red blood cells and epithelial casts with some protein. The blood urea was 100 mg. per 100 ml. A week after admission she became very drowsy and confused, and remained in this state until her death five days later. *Clinical diagnosis:* acute type I nephritis.

At necropsy there was pallor and oedema of the extremities. Death was due to bronchopneumonia. The heart was normal and weighed 300 g. There were a few petechiae in the stomach. The kidneys were enlarged (right 280 g., left 260 g.), soft, and pale, but their pattern was normal. *Pathological diagnosis:* early type II nephritis.

Case 2.—A boy aged 13 was admitted complaining of swelling of the face and legs for a week. At the age of 9 he had had an attack of tonsillitis followed by an illness in which he had headache and pyrexia. He remained in indifferent health, and three months later was admitted to Queen Mary's Hospital, where nephritis was diagnosed. He remained in hospital for six months and then spent six months at home. After this he was again in Queen Mary's for a further six months, and was then admitted to Guy's. He improved greatly on a high-protein diet and was discharged after ten months' treatment. He remained in reasonable health for about a year, although he had several attacks of oedema, each lasting a few days. A week before his last admission he had an attack of macroscopical haematuria, for which he was referred to hospital. On examination he had marked facial, abdominal, and peripheral oedema. His urine contained 10 parts (Esbach) of protein per litre and blood ++. The blood urea was 48 mg. per 100 ml. After a transitory improvement he became progressively worse, and during the next two months he developed pleural and pericardial effusions. At the time of his death the blood urea was 96 mg. per 100 ml. *Clinical diagnosis:* chronic type I nephritis.

Necropsy revealed gross oedema and pallor. The heart weighed 200 g. and was normal, and there was bilateral bronchopneumonia with empyemata. Both kidneys were enlarged, each weighing 225 g. The pattern was preserved and there was yellow streaking of the renal substance. *Pathological diagnosis:* type II nephritis.

Case 3.—A man aged 34 was admitted, having had headaches, vomiting, and blurred vision for two months. When aged 20 he was admitted to Guy's with a story of symptomless haematuria on three occasions, each lasting a week, and of a fourth attack associated with malaise. On examination then he was slightly pyrexial but had no oedema. The blood pressure was 130/80 mm. Hg. His urine (sp. gr. 1025) was bright red with blood, and contained 4 parts (Esbach) of protein per litre. He remained in hospital in bed for the next 50 days, during which time his urine was tested daily. It showed a gradual return to normality except for the persistence of a trace of protein. On only one occasion were pus cells noted. The level of the blood urea on admission was 45 mg. per 100 ml. A diagnosis of acute nephritis was made, and he stayed in hospital for 12 weeks. He remained in good health for the next 13 years, when, two months before his last admission, he was found on examination to be drowsy, with a brown dry tongue and a blood pressure of 240/145 mm. Hg. Papilloedema was present. His urine contained 3 parts (Esbach) protein per litre, the specific gravity varied only from 1008 to 1010, and a few red cells were present, but no casts or pus cells. Urine cultures were sterile and the blood urea was 150 mg. per 100 ml. When he died in a coma one month later the urea had risen to 300 mg. per 100 ml. *Clinical diagnosis:* chronic type I nephritis.

At necropsy the body was pale and there was marked cardiovascular hypertrophy, the heart weighing 550 g. The kidneys were very small (right 30 g., left 50 g.) and the pattern was completely destroyed. The surface was coarsely granular and scarred, and numerous cysts were present. *Pathological diagnosis:* chronic pyelonephritis.

Case 4.—A man aged 58 was admitted complaining of breathlessness and haemoptysis, later shown to be due to pulmonary tuberculosis. He died four months later. He had acute nephritis when aged 23, and at 37 was admitted to St. Olave's Hospital with oedema of the

face, eyes, and legs. A diagnosis of chronic nephritis was made, but unfortunately the records of this admission were destroyed by enemy action. When aged 56 he was admitted to St. Olave's for indigestion, which was shown to be due to a gastric ulcer. Pulmonary tuberculosis and chronic nephritis were also present at this time. His blood pressure was 240/130 mm. Hg. The urine (sp. gr. 1010) contained protein, a few epithelial casts, and some red cells. On admission to Guy's his blood pressure was 245/110 mm. Hg; protein was still present in his urine, but its specific gravity was 1020. The level of blood urea was 66 mg. per 100 ml. *Clinical diagnosis* of the renal condition: chronic type I nephritis.

Necropsy showed advanced bilateral chronic respiratory tuberculosis, and death was due to two large cerebral haemorrhages, one in the right basal ganglia and the other in the pons. Marked cardiovascular hypertrophy was present, the heart weighing 517 g. The kidneys were slightly reduced in size and unequal, although not greatly so (right 97 g., left 107 g.). There was slight capsular adhesion to the finely granular surfaces. The pattern was substantially normal and there was an increase in pelvic fat. The renal arteries were atheromatous. *Pathological diagnosis:* benign nephrosclerosis.

Case 5.—A man aged 30 enjoyed good health until 18 months before his admission, when he developed headaches and vomiting. He had never been ill in his life before, and there was no family history of hypertension. On examination his blood pressure was 220/170 mm. Hg and papilloedema was seen. His urine had a fixed specific gravity of 1010 and contained protein +++ with some granular and hyaline casts and a few pus cells. No red cells were seen. The blood urea on admission was 75 mg. per 100 ml., and rose to 111 mg. per 100 ml. before his death in coma one month later. This man was in the malignant phase of hypertension. In the absence of any family history the occurrence of the condition at this age was probably due to renal disease. There was no history of this, but the urine was more typical of type II nephritis than of primary malignant hypertension. *Clinical diagnosis:* probable type II nephritis with malignant hypertension.

At necropsy pallor and slight oedema were found, along with cardiovascular hypertrophy and bilateral basal bronchopneumonia. The kidneys were of normal size, and each weighed 150 g. The pattern was completely destroyed, the cortex was very thin, and there were some yellow streaks in the renal substance. *Pathological diagnosis:* chronic type I nephritis.

Case 6.—A man aged 30 was admitted complaining of loss of energy and cramps in the calves for about six weeks. For some time he had noticed puffiness of the face and had had nocturnal frequency. The illness started with a coryza and nasal catarrh, and later he developed a sore throat, caused, he thought, by energetic nasal douching with strong saline. This persisted while the other symptoms developed. On examination he was sallow and his face was puffy. His tongue was brown and his mouth dry. The blood pressure was 120/80 mm. Hg, and the urine, which always contained protein, was acid in reaction and had a specific gravity of 1011. Red cells were seen microscopically on only one occasion. The blood urea was 393 mg. per 100 ml. Ten days after admission parotitis developed on the right side and he died a week later. *Clinical diagnosis:* type II nephritis.

At necropsy parotitis was present and there was some oedema of the brain and meninges. The cardiovascular system was normal. There was extreme hydronephrosis on the right side and some large cysts were present in the kidney substance, which was less than a centimetre thick. The left kidney was very small, and had a granular surface and some small cysts. *Pathological diagnosis:* Chronic pyelonephritis.

Case 7.—A woman aged 60 was admitted with a right-sided hemiplegia. She had suffered from mental deterioration for three years, and for three weeks before the stroke she had been treated in bed for heart failure. Before this she had enjoyed good health. Her mother had also had senile mental deterioration and had died from a stroke. On examination her blood pressure was 195/95 mm. Hg; her urine contained protein ++, granular and cellular casts, some red cells, and had a specific gravity of 1025. She died without regaining consciousness. *Clinical diagnosis:* arteriosclerosis with benign nephrosclerosis.

At necropsy there was marked cardiovascular hypertrophy and sclerosis, the heart weighing 500 g. The kidneys were slightly enlarged, and there was some increase in pelvic fat. The pattern was obscure. Some scarring was seen, and there were cysts in the cortex and slight capsular adhesion. *Pathological diagnosis:* type I nephritis.

Clinical Discussion

No difficulty was experienced in the diagnosis of type I nephritis, and clear cases of type II nephritis were also seen. There were, however, cases in which there was abundant information in the notes, but which did not fit easily into this classification. Thus in five of the cases in Table IV—that is, those recorded as Type II (probable)—there was no record of oedema although the clinical story and laboratory findings were otherwise typical.

In his Table I Ellis (1942) showed that his type I nephritis of abrupt onset was clinically distinct from the insidious type II. Similar tables could, however, be constructed for rheumatism of abrupt onset (acute rheumatic fever) and the insidious form of that disease (chronic rheumatic heart disease), but would not be held to separate them aetiologically. Further, in distinguishing type II nephritis from chronic type I no mention is made of the possibility of mild attacks of acute nephritis passing unnoticed, although the paucity of signs and symptoms in some cases that are so recognized and the frequency of acute tonsillitis make the common occurrence of subclinical attacks highly probable. The incidental discovery of three cases of type I nephritis at necropsy during a period in which 30 cases were diagnosed clinically (10%) supports this possibility. Moreover, the clinical features of type II nephritis are much less precise than those of the clearly recognizable type I, so that the former diagnosis may well be applied to various different renal conditions having in common the absence of an acute mode of onset.

Thus it seems that Ellis's contentions must depend for their support upon the existence of a characteristic individual and mutually exclusive histology in his two types.

Pathological Discussion

The main argument against any classification of nephritis is that there is often considerable overlapping of the features presented by a series of cases. There is no doubt that the separate histological pictures described by Ellis do occur in pure form, and the sections here studied contain some unequivocal examples of each. In many kidneys, however, we have found some of the features of several lesions. In particular, the subendothelial hyalinization of the capillaries, characteristic of the type II lesion, was encountered in some degree in ischaemic and other kidneys unassociated with a history of nephritis, and in a case of clinically typical acute nephritis the earlier stage of "bland focal necroses" (Ellis, 1942) was seen. Somewhat similar changes have also been seen in routine necropsy sections from apparently unrelated conditions such as scleroderma and exfoliative dermatitis (one case of each). Seven of our cases also confirm Davson and Platt's (1949) finding of both type I and type II lesions in the same kidney. Agreement had, however, been reached in all these cases, three being diagnosed as type I and four as type II on the basis of the numerically predominant lesion in a glomerular count.

Ellis's method of subdividing these cases pathologically was not, therefore, found entirely satisfactory; neither was the apparent simplicity of the classification paralleled by a comparable ease of microscopical diagnosis.

General Discussion

Highly significant agreements have been found between clinical and pathological diagnoses made on Ellis's criteria after great care had been exercised to avoid collusion. We must conclude, therefore, as did Davson and Platt (1949), that his classification does fit the observed facts. This does not, however, necessarily imply that the features of types I and II require acceptance in every particular. Indeed, it may mean no more than that the less dramatic clinical stories are associated with the less remarkable pathological pictures. Thus while the percentages for the chronic inflammatory diseases shown in Table II (4) represent significantly more agreements than would be obtained by chance, they clearly do not in our hands imply a very high degree of diagnostic accuracy. The independent operation of personal factors may be very important here and cannot be allowed for other than by examining an adequate series with sufficient care. It is of course common experience that any case of more than ordinary complexity may, in the hands of different clinicians and different pathologists, give rise to widely differing opinions as well as to discrepancy between the *ante mortem* and *post mortem* diagnoses; but we believe that the nature of these 154 cases and the materials on which our diagnoses have been based are such that our conclusions are unlikely to be very different from those of other observers making use of the same criteria. If this is so the figures quoted strongly suggest that these criteria may not have been exclusive enough.

It seems to us, therefore, that Ellis's types I and II of nephritis are not mutually exclusive entities, but in his Croonian Lectures little attention was paid to this possibility. The more guarded conclusions of Davson and Platt (1949), the fact that in their investigation clinician and pathologist found it necessary to confer before agreement was reached, and their statement that pathological diagnosis was often made by deciding which was the predominating lesion make it clear that in their series there was some evidence in its favour. In particular, their Case 11, in which the changes of malignant hypertension were found in a type II kidney, may be noted—a combination that we also saw in one case.

We think it more probable, therefore, that the different appearances of type I and type II nephritis represent variations in the response of the renal parenchyma to a single disease rather than to entirely different processes. If this be so, and in view of the difficulties experienced in diagnosis, it seems to us that this classification has little to recommend it from a descriptive point of view. We present no new aetiological evidence, but others have already suggested (Davson and Platt, 1949) that some criticisms may be levelled on these grounds. The pathogenesis has not been elucidated, and it is not necessary to specify the pathological lesion present before giving a prognosis to a patient diagnosed clinically. It may be considered preferable, then, to await some aetiological indications, since these are the only basis for a lasting classification, before accepting a new terminology for nephritis.

Conclusions

In our series of 154 fatal cases of Bright's disease we found chronic pyelonephritis to be about as common as all other forms of inflammatory disease. Acute glomerulonephritis occurred fairly often, but we have no data from which to calculate a fatality rate for this condition. We regard it as an entity separate from and probably commoner than the acute microscopical form of polyarteritis nodosa.

We have obtained significant agreements between independent clinical and pathological diagnoses in all the major groups in the classification suggested by Ellis. Those for degenerative disease and for acute type I nephritis were much better than those for chronic inflammatory conditions. Considerable overlapping was discovered between types I and II of nephritis, and only 63% of them were accurately diagnosed.

From these figures we conclude that the Ellis classification does fit this series of cases, but in its most important aspect, the separation of types I and II of nephritis, it so lacks precision that its adoption hardly seems justified.

We found type II nephritis to be renal failure of insidious onset which may be associated with a variety of pathological conditions. These included acute nephritis, pyelonephritis, and hypertensive and polyarteritic renal lesions. Kidneys showing more than one histological feature said to be individually characteristic were common.

For the present, therefore, it seems that there is little reason for departing from the time-honoured procedure of classifying nephritis into acute, subacute, and chronic forms on clinical grounds. Recognition of nephritis—the acute form of which can usually be distinguished—chronic pyelonephritis, and vascular lesions is probably all that can be accomplished on morphological grounds alone.

Summary

A series of 154 fatal cases of Bright's disease occurring in Guy's Hospital between 1931 and 1951 have been examined independently by us, one making a clinical and the other a pathological diagnosis. The diagnoses were compared and an attempt was made to analyse the results statistically.

Of the lesions responsible for fatal Bright's disease, chronic pyelonephritis accounts for a large proportion, and acute nephritis is not uncommon.

Significant agreement between clinical and histological diagnoses was discovered in all groups when the Ellis classification was applied to these cases. Those for chronic inflammatory conditions were, however, less close than for any of the other major forms of renal disease. Considerable overlapping was encountered and diagnosis was often difficult.

Type II nephritis as diagnosed clinically may be due to several different pathological lesions.

For the present it is suggested that the classification of clinical nephritis into acute, subacute, and chronic forms be continued, and that pathological subdivision be restricted.

We wish to thank Dr. W. J. Martin, of the Department of Statistics, London School of Hygiene and Tropical Medicine, for advice and help with the presentation of the data.

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During the twelve months to November 30, 1952, 4,858 children came into the care of the L.C.C., while 4,169 were discharged. On that date there were altogether 8,027 children in care. This represents an increase of about 700 over the previous year, and of 2,300 compared with three years ago. The numbers in the various age-groups were as follows: Under 2 years, 681 children; 2 to 5 years, 1,411; 5 to 15 years, 4,964; and over 15 years, 971. Of the children taken into care during this period, 45 had no parents, 269 were abandoned, 2,637 were taken into care owing to the illness or infirmity of their parents or guardians, and 631 came as a result of "fit person" orders. These figures were given at a meeting of the Children's Committee of the L.C.C. on April 27.

H. PAYLING WRIGHT, M. M. KUBIK, AND M. HAYDEN: RECANALIZATION OF THROMBOSED ARTERIES UNDER ANTICOAGULANT THERAPY

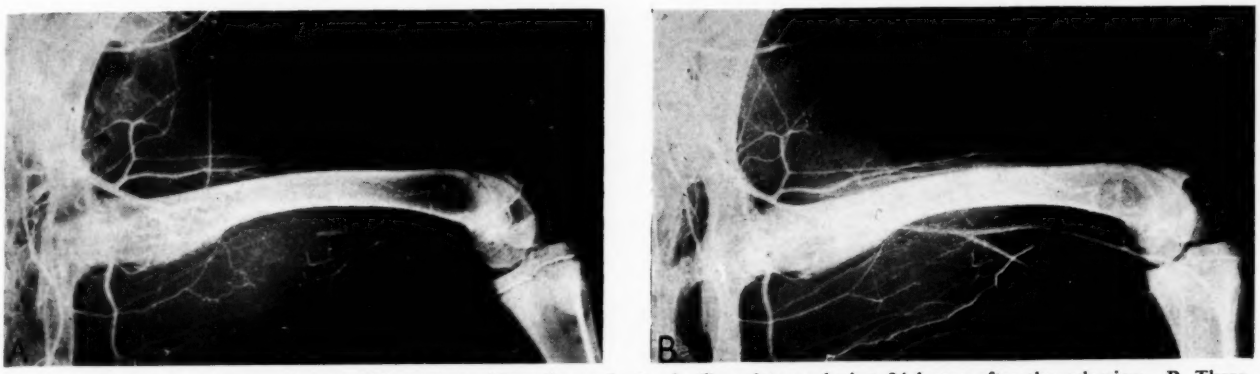


FIG. 1.—Femoral arteriograms from rabbit treated with anticoagulant. A, Complete occlusion 24 hours after thrombosing. B, Three weeks later, artery again patent.

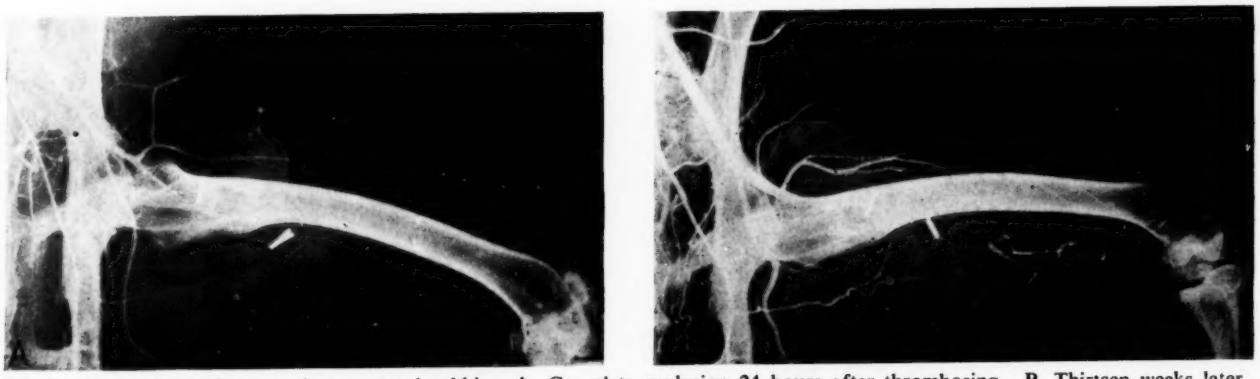


FIG. 2.—Femoral arteriograms from control rabbit. A, Complete occlusion 24 hours after thrombosing. B, Thirteen weeks later, artery still occluded. Development of collateral vessels is marked.

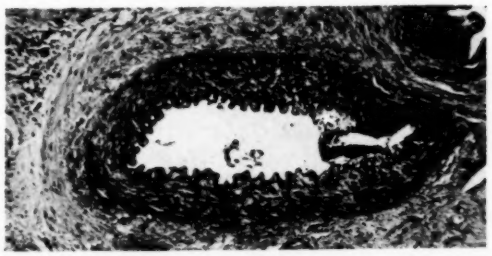


FIG. 3.—Section through femoral artery of treated rabbit at level of thrombus after patency has been restored. (×64.)

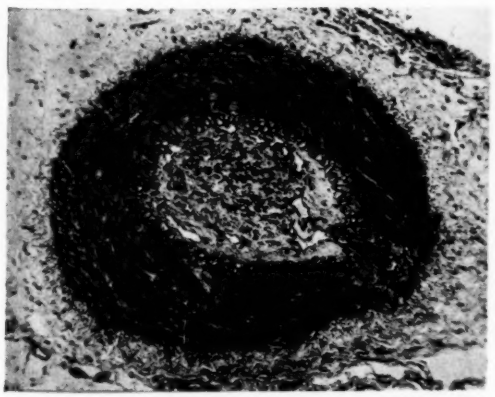
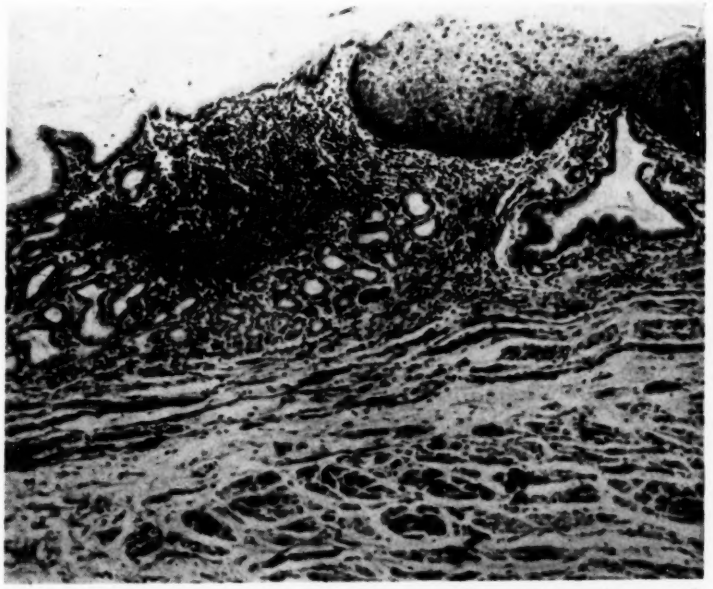


FIG. 4.—Section through femoral artery of control rabbit at level of occlusion. (×64.)

G. RIOS-SOLANS: SLIDING HERNIAS THROUGH THE OESOPHAGEAL HIATUS



Section showing junction of stratified squamous lining of oesophagus and mucous membrane of stomach. (×33.)

J. B. ENTICKNAP AND C. L. JOINER : BRIGHT'S DISEASE

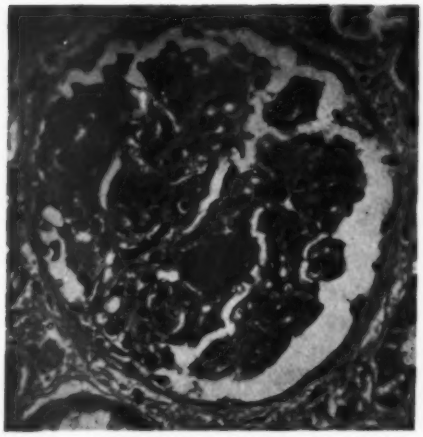


FIG. 1.—Early focal-necrosis stage of type II nephritis in a kidney from a case clinically diagnosed as type I. (H. and E. ×210.)

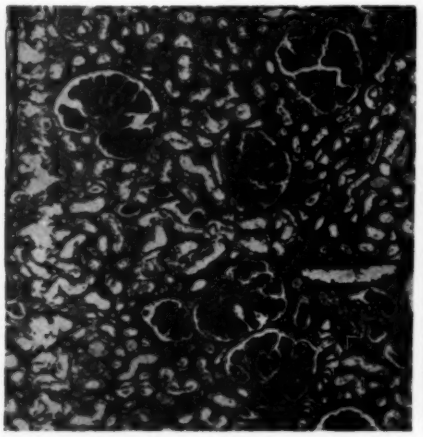


FIG. 2.—Type II nephritis in a case clinically diagnosed as type I. (Mallory. ×50.)

FIG. 3.—Chronic pyelonephritis in a case of type I nephritis. (H. and E. ×16.)

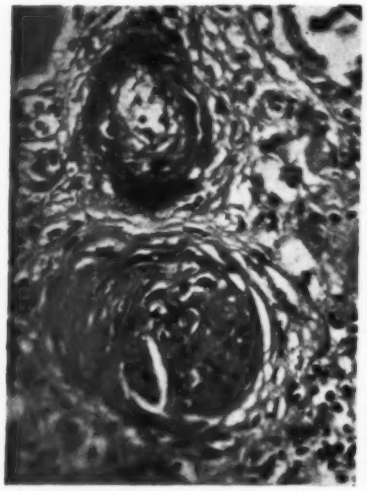


FIG. 4.—Benign nephrosclerosis in a case of type I nephritis. (H. and E. ×200.)

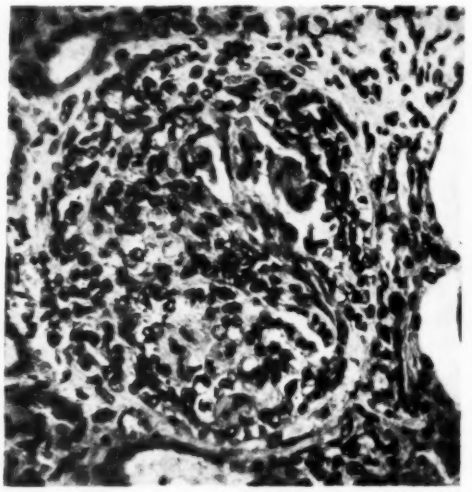


FIG. 5.—Type I glomerular lesion in a case of type II nephritis. (H. and E. ×180.)

FIG. 6.—Chronic pyelonephritis in a case of type II nephritis. (H. and E. ×70.)

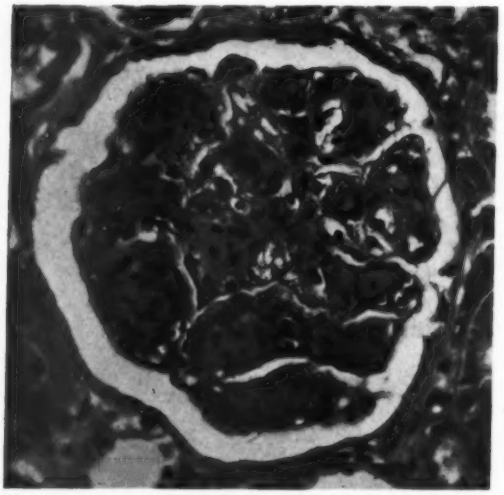
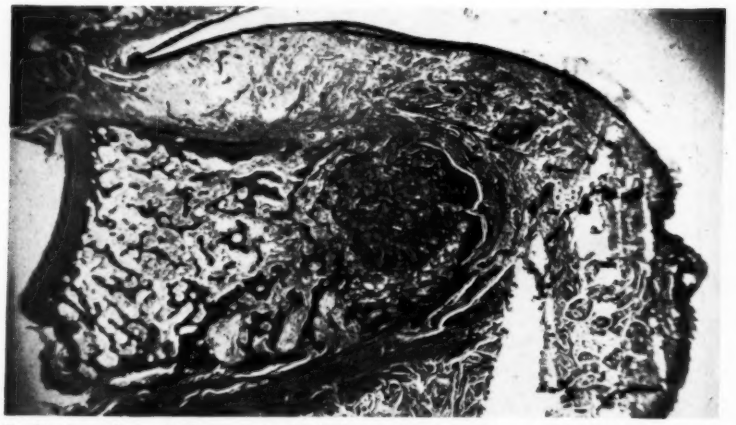


FIG. 7.—Type II glomerular lesion in a case of benign nephrosclerosis. (H. and E. ×200.)

E. H. STRACH : OSTEOID OSTEOMA



Sagittal section of the terminal phalanx showing the osteoid osteoma at the tip. (Low power.)

RECANALIZATION OF THROMBOSED ARTERIES UNDER ANTICOAGULANT THERAPY

BY

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[WITH SPECIAL PLATE]

Arterial occlusion, due entirely or partially to thrombosis, is a result of various pathological processes. In every case, however, it is a serious development which endangers the vitality of the organ or extremity concerned. It is evident that details of treatment must be modified according to the primary disease and the artery affected. Apart from promoting the collateral circulation and other measures designed to balance the disproportion between blood supply and local oxygen requirements, it is the dissolution or recanalization of the obstructing clot which should be the ultimate aim of treatment.

We have already presented evidence that the rate of recanalization of venous channels which had been thrombosed experimentally was greatly accelerated when the prothrombin activity was adequately lowered by the administration of suitable doses of a dicoumarol anticoagulant (ethyl biscoumacetate, "tromexan") (Wright, Kubik, and Hayden, 1952). Encouraged by the findings in a preliminary investigation upon recanalization of arteries (Kubik and Wright, 1950), a more complete experimental study has been undertaken to assess the value of dicoumarol treatment in thrombosis in these vessels.

Methods

Since it was found that blood prothrombin levels fluctuated considerably during anticoagulant treatment and that doe rabbits often died from uterine haemorrhage, full-grown young bucks were used throughout the following experiments.

Under pentobarbitone sodium anaesthesia the femoral artery was exposed for a length of 2 cm. on one or both sides through a longitudinal incision on the median aspect of the thigh. The stripped length of vessel was lifted on four ligatures spaced about 1 cm. apart, so that its lumen was able to be compressed in three sections. Just enough pressure was applied to the ligatures to prevent the blood flow in the artery while 0.02 ml. of thrombin solution (1,000 units per ml.) was injected through a fine intradermal hypodermic needle into the middle section and 0.02 ml. of 10% sodium morrhuate into the proximal and distal ones. In those animals in which mechanical interference to the vessel had caused arterial constriction, a solution of papaverine sulphate (1.25%) was applied to overcome the spasm (Kinmonth, 1952). The injected substances were maintained in the occluded sections for ten minutes, after which time the pressure on the ligatures was gradually released.

A small flow of blood was occasionally apparent immediately after the release of the pressure, but when fresh blood came in contact with the sclerosed areas and with the local thrombin coagulum, thrombosis occurred within a few moments and could be recognized from the outside of the vessel as a fusiform dark-red section, incompressible when gently pinched.

In our preliminary report (Kubik and Wright, 1950) peripheral gangrene was often found in the foot after thrombosis of the femoral artery. This was possibly due either to injury of the femoral nerve or to thrombosis of the arteries of the foot produced by morrhuate carried peripherally by the blood stream. This complication did not occur with the improved technique described here.

After arterial occlusion the animals were divided into two groups: (A) those which received ethyl biscoumacetate daily by mouth, starting 24 hours after the thrombus had been formed; and (B) those which, as controls, received no treatment. The ethyl biscoumacetate, as a suspension in methylcellulose ("cellofas") (Wright, Kubik, and Hayden, 1952), was given through a short rubber tube, which was passed to the back of the pharynx so that regurgitation could not occur. The dosage was controlled by prothrombin estimations carried out three times a week, using the Quick single-stage technique on blood drawn by ear-vein puncture. The prothrombin time aimed at for every animal was 30 seconds (rabbit normal, 9 seconds), and, to achieve this, doses of 100–300 mg. per kg. body weight were required daily. Prothrombin-level fluctuations in rabbits are, however, both rapid and profound, and in the course of the experiments several animals were lost through concealed haemorrhage into the caecum. Nevertheless, the prothrombin times in the majority were maintained between 25 and 35 seconds throughout the experimental period, and only these animals are included in this report.

An arteriographic technique was used to follow any changes which might occur in the occluded vessel, the first *x*-ray film being taken 24 hours after thrombosing to show the extent of the obstruction. Under pentobarbitone sodium anaesthesia, a 3-cm. midline abdominal incision was made, the gut was held aside within the body cavity, and the aorta was exposed for a length of about 1 cm. A fine hypodermic needle (No. 16), inserted into a polythene tube about 20 cm. long and with a syringe attachment at the distal end, was introduced into the exposed aorta. Through this, 2 ml. of thorotrast, as contrast medium, was injected during a period of 4 seconds and the *x*-ray film was taken while it was still flowing in. Double-wrapped 10 by 12 in. (25 by 30 cm.) "improved fast Ilfex film" with exposure factors of 53 kV, 50 mA, and 0.5 second was used throughout.

Further *x*-ray films were made with the same technique at two-weekly intervals for Group A and at four-weekly intervals for Group B.

Results

It was early apparent that a considerable difference in the time required for the recanalization of the femoral arteries occurred between those animals which received adequate anticoagulant treatment and the untreated controls. In the eight animals in Group A, the average time taken for one or both vessels to become patent was only 3.25 weeks, while in Group B none of the six controls were patent by 8 weeks, and further *x*-ray films taken at various later dates showed no evidence of recanalization at any time. The details of both groups are set out in the Table. Typical arteriograms of animals (Nos. 6 and 10) from each group are shown in the Plate, Figs. 1 and 2.

The criterion of "occluded" or "patent" is, moreover, a stringent one. In Group A, when one artery has become patent, the thrombus in the remaining occluded vessel generally shows a considerable reduction in its length, even though complete patency has not been established. A longer period of treatment would presumably further reduce the size of the occluding mass, if not allow of its entire removal. In the control group, on the other hand, no such changes were evident, the size of the occlusion showing no material diminution; indeed, in one animal (No. 12) which was

Time Taken (Weeks) for Recanalization of Thrombosed Arteries

	Week of X-ray Film	Right Femoral	Left Femoral
Group A (treated):			
Rabbit 1 ..	2½ (died)	O	O
,, 2 ..	4	P	P
,, 3 ..	4	O	P
,, 4 ..	3	O	P
,, 5 ..	2	P	P
,, 6 ..	3	O	P
,, 7 ..	8	—	P
,, 8 ..	2	—	P
Group B (control):			
Rabbit 9 ..	8	O	O
,, 10 ..	13	O	O
,, 11 ..	22	O	—
,, 12 ..	46	—	O
,, 13 ..	12	O	—
,, 14 ..	15	O	—

O=Occluded. P=Patent.

specially kept, the artery was still fully occluded after eleven months. Other animals of this group were destroyed at varying intervals.

Histological sections of arteries from animals of both groups were examined at the end of the experimental period. In the treated group the animal was sacrificed after the patency of the femoral artery had been established by arteriogram. Fig. 3 shows a photomicrograph of the artery from rabbit No. 6, which was open after three weeks of anticoagulant treatment. The intima appears normal except at one point where there is a small residual mural thrombus. The lumen is otherwise free from obstruction.

In the control group histological sections were taken through the vessel at the level of the obstruction. Fig. 4 shows a typical organizing thrombus with fibroblasts and haemosiderin granules in the granulation tissue matrix three months after arterial obstruction had been produced (rabbit No. 10).

Discussion

In comparison with the interest shown in the influence of anticoagulants on experimental venous thrombosis, little attention, so far as we know, has been paid to corresponding changes in arteries. Experimental work on coronary occlusion has been undertaken, but even here the arterial block was produced by ligation of a branch of the coronary vessel. The result of subsequent anticoagulant therapy on the myocardial infarction so produced was described by Beattie and his colleagues (1948). Le Roy and Nalefski (1948) investigated the possible ill effects of dicoumarol on the myocardium, but it is obvious that neither of these groups of workers were interested in the effects of their therapy on the primary occlusion, or the technique of ligation would not have been used.

It is remarkable that, though a considerable number of experiments have established the fact that the administration of dicoumarol or its derivatives reduces the formation of intravascular coagulation (Marple and Wright, 1950), the experimental investigation of the influence of these drugs on preformed thrombi *in situ* has been omitted. Loewe (1947) and Loewe and Hirsch (1947) suggested that the administration of heparin facilitated the reopening of veins recently occluded by fresh unorganized thrombus, but a study of thrombosed arteries has been largely neglected, though it obviously has a wide clinical application.

Experimentally it is difficult to produce conditions similar to those occurring in the majority of occlusive arterial diseases. First, in the naturally occurring process the endothelium undergoes changes which cannot be reproduced in the experimental animal; the actual thrombosis occurs in a vessel previously diseased. Secondly, in clinical practice, except in cases of embolism, the obstruction develops gradually and there is, as yet, no experimental method for producing such a progressive occlusion. In the third place, the inflammatory character of certain of the arterial diseases cannot be fully imitated, though recently Rabinovitch and Pines (1949) have claimed satisfactory results in reproducing this change in veins by injecting staphylococci into the wall of the blood vessel. In our method, using both thrombin, which produces a red coagulum, and morrhuate, which damages the endothelium, we believe that many of the features of normally occurring arterial occlusion are paralleled.

In assessing the results presented here it must be borne in mind that rabbits are relatively resistant to the coumarin group of anticoagulants. Their plasma possesses a considerably greater prothrombin activity than that of human blood (Quick, 1936). Larger doses and more prolonged treatment are consequently needed to influence their prothrombin levels to correspond with the human equivalent. In these animals, moreover, wide fluctuations of prothrombin activity while receiving coumarin treatment make it difficult to maintain them at an adequate level without the risk of haemorrhage. The results which we have obtained, however, make it clear that the administration of the anticoagulant has, under the conditions of our experiments, the effect of promoting the recanalization of the thrombosed lengths of the arteries.

How this effect is brought about is still uncertain, but in a previous paper (Wright, Kubik, and Hayden, 1952) we described our findings and suggested a possible mode of action of ethyl biscoumacetate on venous thrombi. The increased rate of recanalization observed is possibly due to the normally continuous action of fibrinolysin, which is usually masked by the continual deposition of small quantities of fresh fibrin on the thrombus surface, and which is disclosed in the presence of anticoagulant when fibrin deposition is prevented. The action of the anticoagulant would therefore appear to be an indirect one.

From preliminary experiments it was found more difficult to thrombose an artery than a vein, but once occluded it remained so. We did not observe any spontaneous recanalization in our control group even after many weeks. In the light of this it is difficult to explain the disappearance of the arterial thrombus with ethyl biscoumacetate treatment wholly by its indirect action. Schmid and Stockinger (1951) observed that dicoumarol, and still more ethyl biscoumacetate, significantly depressed the growth and dividing power of fibroblasts in tissue culture. This effect was present even in the low concentrations found in the blood during anticoagulant therapy. It is therefore possible that the organization of the thrombus is modified by these drugs, and this plays a leading part in promoting the recanalization of the intra-arterial thrombus.

Application of experimental data to human pathology is always somewhat hazardous. The conclusion seems justified, however, that adequate prolonged treatment with dicoumarol in general and with ethyl biscoumacetate in particular has a favourable influence on the reabsorption of arterial thrombi, provided therapy is started soon after occlusion has occurred. Such treatment may result in reopening of the occluded vessel when the obstruction is due to thrombotic and not to arteriosclerotic changes.

Summary

A method for producing thrombi in rabbits' femoral arteries is described.

The time taken for recanalization to take place in control and anticoagulant-treated animals was recorded by arteriography.

The treated group showed an average recanalization period of 3½ weeks, while the controls were still occluded after several months.

The influence of anticoagulant treatment is dependent upon the maintenance of a low prothrombin level.

A discussion of the possible mode of action is offered.

We wish to express our thanks to Dr. C. J. Hodson and to members of the *x*-ray diagnostic department for their help with this work.

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METABOLIC CHANGES ASSOCIATED WITH OPERATION*

BY

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That the recovery from injury follows a recognized pattern has been known from very early times. This was clearly appreciated by John Hunter (1794). In 1872 Bauer observed that an increased elimination of nitrogen followed upon haemorrhage, and Hawk and Gies (1904) showed that the actual operation of venesection without withdrawal of blood was enough to cause increased urinary output of nitrogen and sulphur. This increased nitrogen loss was also noticed by Benedict (1915) during prolonged starvation. Since that time many observers have noted this increased nitrogen catabolism as a result of injury, associated with increased phosphorus, sulphur, and potassium loss (Cuthbertson *et al.*, 1939 ; Cuthbertson, 1942 ; Wilkinson *et al.*, 1949). The varying nature of the injuries causing this has tended to emphasize that something inherent in the trauma, or some underlying response, might be common to many and various injuries done to the body, and deprivations to which it might be exposed.

Wilson and Stewart (1939) noted that, in burns, sodium was lost from the extracellular fluids into the cells of the damaged tissues, and also into the erythrocytes of the general circulation. The observations of Cuthbertson *et al.* (1939) on the urinary excretion of potassium and nitrogen led them to believe that the increased excretion of these substances was due to muscle catabolism following operative injury, but they noted that potassium was lost in greater proportion than nitrogen when compared with their relative concentrations in muscle protoplasm. Howard *et al.* (1946) have also shown that the nitrogen, potassium, sulphur, and phosphorus loss is not proportional to their content in muscle, and that the greatest potassium loss occurs in the first 24 hours. Blixenkrone-Møller (1949) demonstrated that the maximal potassium loss after operation precedes the maximal nitrogen excretion.

Wilkinson *et al.* (1950) demonstrated that after surgical operation potassium is lost in the urine in high concentration when the potassium intake is low, that the loss is greatest in the first three days after operation, and that it precedes in time the nitrogen loss, which persists throughout the first post-operative week. In a previous paper Wilkinson *et al.* (1949) had drawn attention to the marked retention of sodium and chloride in the early post-operative period, occurring at the same time as the phase of increased potassium loss. Annersten and Norinder (1946) had previously observed a slight reduction in serum sodium and chloride after operation. They did not believe that these changes were significant. Similarly Wilkinson *et al.* (1951) noted such slight changes, but again did not believe them to be an explanation of the retention of sodium and chloride after operation.

I first became interested in this problem in 1948, when I observed the retention of chloride and of sodium after operation. The effect was thought to be very similar to the results of the administration of 11-deoxycorticosterone acetate (D.C.A.). In view of the observations of Hans Selye, it was believed that these electrolyte changes might well be due to increased adrenocortical function following the stimulus of operation. It was decided to observe these changes again and, at the same time, to measure adrenocortical function.

Results

Electrolyte Changes

Fig. 1 shows the typical features of the electrolyte changes in the plasma and urine before and after operation. In all cases a great reduction in the excretion of sodium and of chloride in the urine was observed immediately following operation ; this persisted for about seven days. After this, the sodium and chloride excretion in the urine tended to rise above the pre-operative level. Associated with these changes, a constant but much diminished fall in serum sodium and plasma chloride was detected during the same period. A return to the pre-operative level occurred about the end of the first week.

During the same period the serum potassium concentration appeared to be variable and showed no pronounced change. In general, the concentration of potassium in the

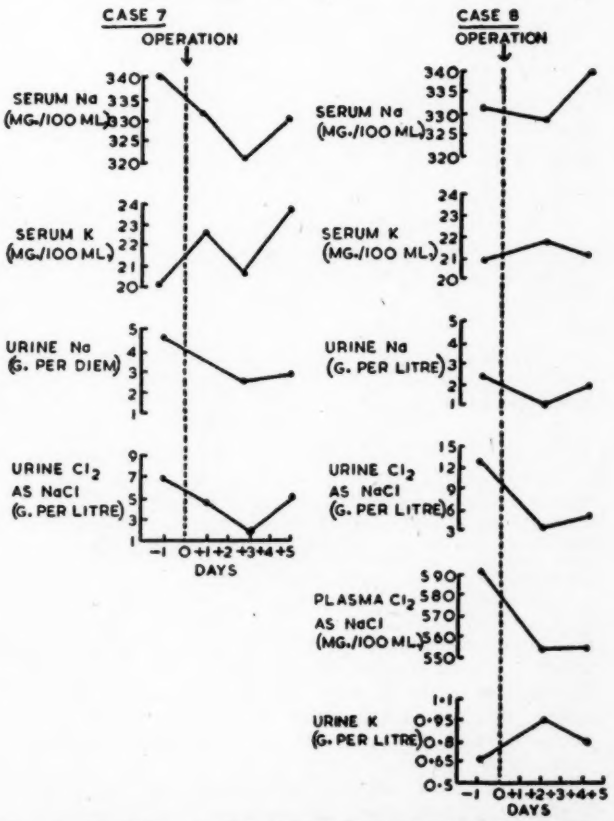

FIG. 1.—Typical examples of electrolyte changes in blood and urine.

*Part of a thesis submitted for the degree of M.D. of the University of Glasgow.

serum was slightly elevated during some part of the post-operative period. Fig. 2, a composite diagram of the potassium excretion of another series of eight cases under the same conditions, demonstrates the continued loss after operation of potassium in the urine during the period of negligible potassium intake. The increased excretion of potassium appears to decline after the third post-operative day.

From the previous work discussed above, and as a result of observations made in the present study, it seems that after operation a reduced excretion of sodium and chloride is to be expected, associated with an increased excretion of potassium. The changes in the blood, however, are not so well established. As has been stated, the decrease in plasma chloride and serum sodium immediately after operation observed by Annersten and Norinder (1946) and by Wilkinson *et al.* (1951) was not considered by them to be significant. The changes in serum sodium of the nine cases of the present series are typically represented by those shown in Fig. 1. The majority are greater than the experimental error of the method used, and, though small, seem to be none the less real. This applies also to the plasma chloride changes detected in ten patients. Since the potassium lost must, in the end-result, be derived from cell potassium, it was thought that the small apparent loss of sodium and chloride in the body fluid after operation, at a time when the body is retaining sodium and chloride, might be due to a replacement of cell potassium by sodium and to an increase in cell chloride. Fig. 3 shows the results of the study of erythrocyte sodium and plasma sodium in another series of six patients. In four of the cases the estimations were made on the day before and after operation. The results show that the decrease in plasma sodium after operation equalled almost exactly the increase in cell sodium (Fig. 3, A and B). In two of the cases the estimations were performed on the day of operation, and on the fourth post-operative day (Fig. 3, C and D). By this time the changes had been reversed; the cell sodium content was now below the pre-operative level and the plasma sodium was above the pre-operative level.

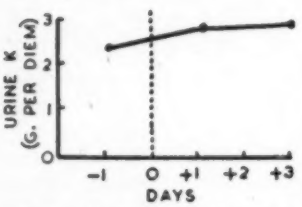

FIG. 2.—A composite diagram of the urinary potassium excretion during the early post-operative phase in eight cases.

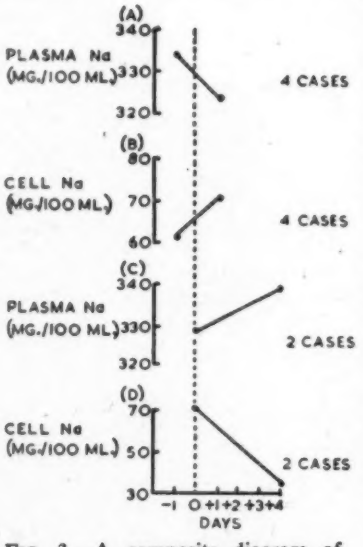

FIG. 3.—A composite diagram of erythrocyte and plasma sodium, in four cases on the day before and after operation, and in two cases on the day of operation and the fourth post-operative day.

Similar estimations of cellular and plasma potassium were undertaken on these patients, but no constant and appreciable changes were detected. Though no conclusion can be deduced from this small experiment, it does suggest that the slight decrease in serum or plasma sodium after operation is due to that amount of sodium entering the tissue cells.

Body Water Changes

Blood Volume.—(a) Haemoglobin and haematocrit estimations:—At the same time as the observations were made on electrolyte changes, some estimations of any changes to be detected in the body water were also made. Fig. 4 shows the pre- and post-operative haemoglobin and haematocrit levels in the original nine patients of the series. There seem to be two distinct reactions in this series. As would be expected following any haemorrhage, five patients show evidence of haemodilution. The second group of four patients, under the same circumstances, show evidence of haemoconcentration. (*b*) *Plasma volume:* In only two patients of this series was the plasma volume determined by the dye method. No significant reduction in plasma volume was detected. (*c*) *Plasma proteins:* Estimations were undertaken in five patients before and after operation. In four the total plasma protein content was reduced, and in one the increase was not significant. As will be seen from the Table, there was a general reduction in both the albumin and the globulin fraction after operation. (*d*) *Blood pressure:* These recordings were made in five patients in whom any degree of post-operative shock could be definitely excluded. No significant alteration in blood pressure, except on the day of operation, was noted in any case.

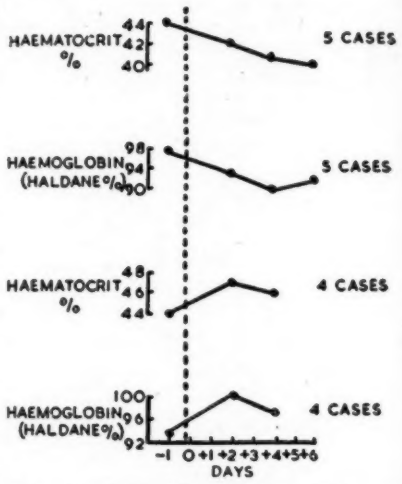

FIG. 4.—Composite diagrams of haematocrit and haemoglobin levels, showing the two different types of reaction.

Plasma Protein Content Before and After Operation

Day:	−2		−1		0		+1		+2		+3	
Case	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.	Alb.	Glob.
27	3·9	3·2							4·7	1·5		
28					4·5	2·1			4·8	2·3		
29			5·0	2·3			4·8	2·3				
30					4·6	2·4					4·6	2·2
31			5·0	2·7					4·2	2·0		

Extracellular Fluid-space Volume.—This was estimated in only two patients, using sodium thiocyanate. As only relative changes were to be considered, the inaccuracy of the "thiocyanate space" as a measure of the extracellular fluid space was not important. No significant change was observed after operation.

Total Body Water.—Because more elaborate methods, such as the use of deuterium oxide, were not available, changes in total body water were estimated by means of changes in body weight. Fig. 5 shows a typical example of the changes in body weight, measured in pounds, following operation in patients weighed at the same time each day, in the same clothing, on the same machine, and after a 12-hours fast. A weight loss is noted in three of the cases, a gain in three, and no change in one case. The daily weight loss for the average

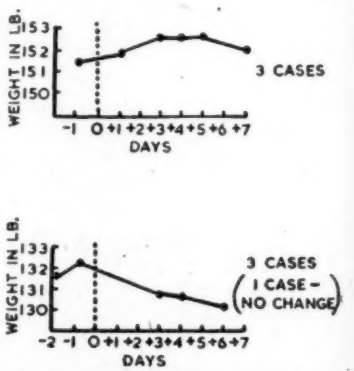

FIG. 5.—Composite diagrams showing changes in body weight.

male during starvation and without water depletion has been estimated as about 260 g., or 9 oz. (Wright, 1940). If after operation the nitrogen loss is even greater than in starvation alone, a still greater weight loss might be expected. Any weight gain or maintenance of previous weight must therefore be a measure of water retention within the body. Four of the seven cases appear, therefore, to show a water retention after operation.

Urine Volume.—In this paragraph only urinary volume studies are under review. Fig. 6 is a composite diagram of the average daily fluid intake and urine output of the nine patients. Except for the day of operation, the urine output in the first six days after operation appeared to remain remarkably constant in these adequately hydrated patients. During the next four days the urine output increased, and approximated to the fluid intake.

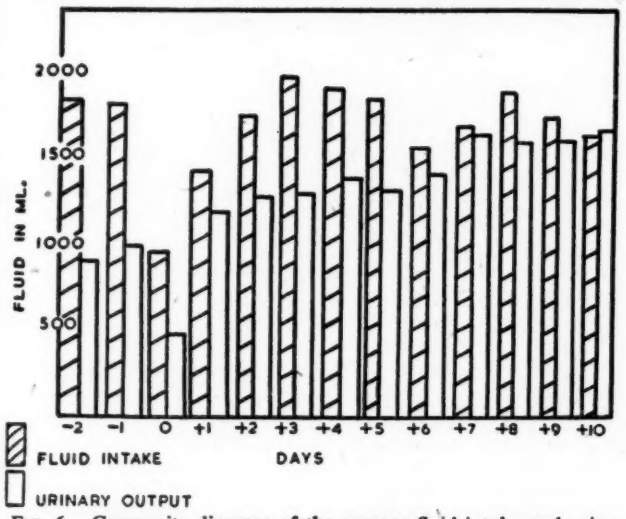

FIG. 6.—Composite diagram of the average fluid intake and urine output of the nine cases.

Evidence of Increased "Glucocorticoid" Activity

The tests used here to measure increased secretion of corticoids are not necessarily the best for the purpose, but simply those most suitable for performing as routine estimations in a teaching hospital.

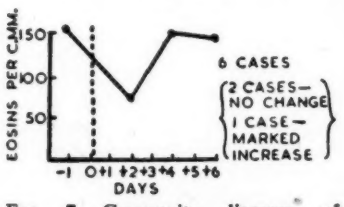

FIG. 7.—Composite diagram of circulatory eosinophil counts in six of the nine cases.

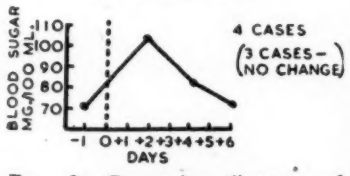

FIG. 8.—Composite diagram of blood-sugar changes in four of the seven cases in which sugar determinations were made.

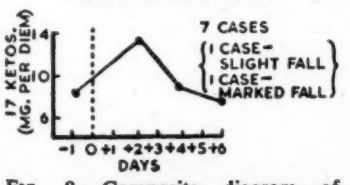

FIG. 9.—Composite diagram of urinary 17-ketosteroid excretion a day in seven of the nine cases.

Eosinophil Counts.—Fig. 7 is a composite diagram of circulatory eosinophil counts before and after operation in those patients whose electrolyte and water balance was also under observation. In six of the nine patients a marked fall in the eosinophil count took place in the immediate post-operative period, in two little variation was detected, and in one case only was there a marked rise after operation. After the initial fall a rise in the post-operative phase was observed in five of the six cases.

Fasting Blood-sugar Levels.—After a 12-hours fast, and in the resting state, blood-sugar determinations were made in seven of the nine patients. Fig. 8 shows the blood-sugar levels in four of the seven patients. These four patients showed a considerable rise in blood sugar in the immediate post-operative phase. The remaining three patients had no change in the blood-sugar levels after operation.

It is interesting to observe that, of the three patients in whom there was no evidence of decreased eosinophil counts after operation, one showed increased blood-sugar concentration after operation. Further, of the three patients who showed no evidence of an increase in blood sugar after operation, all showed a considerable fall in eosinophil counts. Thus, applying both tests, only two patients did not give any evidence of increased "glucocorticoid" activity after operation.

Evidence of Increased Androgen Formation

17-Ketosteroid Excretion.—Fig. 9 is a composite diagram of the excretion of 17-ketosteroids a day in the urine following operation. Seven of the nine cases showed evidence of increased 17-ketosteroid excretion on the first or second day. The increased ketosteroid excretion in these cases tended to fall below the pre-operative level by about the sixth day. Of the two cases which did not show an increase in ketosteroid excretion after operation, one was excreting 17-ketosteroids at the upper limit of normal in the pre-operative phase. This was followed in the early post-operative period by a marked fall, followed by a sharp rise again on the fourth day.

Discussion

The Electrolyte Changes

The reduction in the excretion of sodium and chloride in the first week after operation, and the increased excretion of potassium previously noted by Blixenkrone-Møller (1949) and by Wilkinson *et al.* (1949, 1950, 1951), are confirmed in the present series. This study also indicates that these features are common to relatively minor surgical procedures, where no intravenous electrolyte or blood replacement therapy has been undertaken either at the time of operation or thereafter. Gamble (1942) has shown that the intravenous infusion of saline is sufficient, by itself, to cause an increased excretion of potassium in the urine. This factor can be excluded in the present series.

It would seem that the increased excretion of potassium after such operations is a phenomenon similar to the increased potassium excretion following operative fracture of the long bones, as demonstrated by Cuthbertson *et al.* (1939). Cuthbertson (1942) considered this to be part of an intimate response of the organism to trauma. His findings, and those of Wilkinson *et al.* (1950), indicate that the potassium loss after operation occurs to a degree greater in proportion than the nitrogen loss, that it precedes the nitrogen loss, and that it terminates before the phase of negative nitrogen metabolism has ceased. Blixenkrone-Møller has detected an increased potassium excretion within six hours of operation. Benedict (1915) and Howard *et al.* (1946) have shown that the potassium loss during starvation and in progressively diminishing diets is directly proportional to the nitrogen loss when compared with the concentration of both substances in muscle.

It would appear, therefore, that factors over and above rest in bed and starvation are effective in causing the sodium and chloride retention and increased potassium excretion associated with operation. Selye (1950) believes that these electrolyte changes are a part of the "stress" response, and partly due to an adrenocortical response to injury. Similar retention of water and salt with increased excretion of potassium is observed after the injection of 11-deoxycorticosterone acetate (D.C.A.) in animals (Ferrebee *et al.*, 1941), and in man (Ingle and Thorn, 1941), and also after the administration of A.C.T.H. (Forsham *et al.*, 1948; Mason *et al.*, 1948; Elkinton *et al.*, 1949).

The Cellular Electrolyte Changes

The older concepts that the cell membrane offered an impermeable barrier to the passage of sodium and potassium is now known to be incorrect. Maizels (1949) has shown that in blood stored at 37° C. an active expulsion of sodium from the cell takes place, accompanied by an uptake of potassium. Mullins *et al.* (1941) have shown the rapid penetration of the erythrocyte by radioactive potassium, and to a less extent by sodium, in three hours. During anaerobic metabolism, in the absence of glucose, the potassium concentration of the serum (Danowski, 1941), or the brain-tissue fluid (Dixon, 1949), has been shown to rise, owing to a loss of potassium from the cells of the respective tissue. Ferrebee *et al.* (1941) have shown clearly that, in dogs, symptoms of cellular depletion of potassium may arise after the administration of D.C.A. It has also been shown that in animals fed on a low-potassium and high-sodium diet partial replacement of deficient cellular potassium can be induced by increase in cell sodium (Heppel, 1939; Miller and Darrow, 1940). Fenn and Cobb (1936) found that after prolonged indirect stimulation of muscles in anaesthetized rats, potassium was lost from the muscle cells and replaced by sodium. After two hours' rest these changes were reversed, indicating that no permanent damage had been done to the muscle.

From all these observations there is strong experimental and clinical evidence to show that potassium and sodium, under certain circumstances, may be interchangeable across the cell membranes. Such an interchange would account for the increased potassium excretion following operation. It would also account for the relatively slight fall in the serum sodium and chloride observed here, and considered not significant by Annersten and Norinder (1946) and by Wilkinson *et al.* (1951). The short study of intracellular electrolyte in the present series confirms this conclusion—an increased erythrocyte sodium content being observed in the immediate post-operative period, and the plasma sodium being reduced by the corresponding amount. No change was noted in the erythrocyte potassium content. This does not invalidate the assumption that the potassium has been derived from tissue cells, as demonstrated by the workers already cited.

The question why potassium should leave the cell under a variety of circumstances seems to be open to two interpretations. Gamble (1942) believes that, in conditions of clinical dehydration, water and potassium pass out from the cell, depending upon the changes in extracellular fluid and electrolyte. In the present series of cases no question of extracellular dehydration arises. Indeed, it has been shown that water and electrolyte, probably in equal relative proportion, are retained within the body.

Another concept, which seems to fit the facts in a more extensive range of conditions leading to the same end-result, has been suggested by Maizels (1949). It is indeed curious that the normal cell-to-tissue cation equilibrium should remain established at any time. As Maizels has indicated, this accumulation of potassium in the cell against the concentration gradient has long been a cause for speculation. Maizels, from his own observations, does not believe that an active excretion of sodium from the cell requires an active absorption of potassium. He believes that potassium passes into the cell passively, and secondarily to the active expulsion of sodium.

It would therefore seem that, following operation or trauma, the relative permeability of the cell-membrane is altered, potassium is liberated, and any tendency to a marked rise in extracellular potassium is prevented by the rapid excretion of that ion in the urine. Either, to replace this cell base, sodium appears to enter the cell from the surrounding extracellular fluid, or else, if Maizels's view is accepted, the "pumping" mechanism breaks down, sodium is not sufficiently expelled from the cell, and perhaps, to maintain the correct osmotic tension, potassium leaks out into the tissue fluids.

Alterations in Body Water

Plasma Volume.—Wilkinson *et al.* (1951), in a series of 10 cases, demonstrated a decrease in plasma volume immediately after operation—directly by the dye method (T 1824) and indirectly by changes in haemoglobin and haematocrit readings. Studies of plasma-protein fractions indicated that this was due to a reduction in plasma albumin and an increase in plasma globulin. These results, in association with some of the electrolyte changes considered above, led them to suggest a transudation of water, albumin, sodium, and chloride into the tissues at the site of injury. Their cases all received blood transfusion at the time of operation, and were undergoing major surgery. In the present investigation the direct plasma-volume studies were not extended sufficiently to be of any value. So far as indirect mensuration may be of value, five of the patients showed evidence of haemodilution in the immediate post-operative phase and four showed evidence of haemoconcentration. No confirmation of a relative reduction in plasma albumin with an increase in globulin was obtained.

Extracellular Space Volume.—Wilkinson and his associates, in their study of the total extracellular space volume in the same cases, did not observe any regular change in the post-operative period. The studies in the present paper are too few to be of value, but they do tend to confirm this finding.

Total Body Water.—As has been shown in the present series, evidence has been obtained of an increase in total body water in some of the cases. Whether this is due to an increase in the extracellular extravascular space as determined directly by Wilkinson and his associates, or whether it is due to an increase in cellular water, has not been determined here. As Darrow has shown (Gamble, 1942), the excretion of potassium in infantile diarrhoea is associated with cellular dehydration. On the other hand Fenn and Cobb (1936), in their experiments on continued muscle stimulation, showed that the passage of sodium and chloride into the cells was associated with an increase in the intracellular water space.

Urine Volume.—The gradual approximation of the urine excretion to the fluid intake late in the post-operative period would tend to suggest that a water retention had occurred at an earlier stage. The relative diuresis for each patient seems to occur on a different day after the first post-operative week. For this reason the combined chart masks this relative diuretic effect.

Evidence of 11-Oxysteroid Activity

Eosinophil Counts.—Forsham *et al.* (1948) and Carlisle (1950) have indicated that both A.C.T.H. and cortisone depress the circulating eosinophil count. Cope *et al.* (1951) point out that it is specifically cortisone and 17-hydroxycorticosterone which exert this influence in the adrenalectomized animal. The depression of the eosinophil count, provided the reduction is at least by 50%, has often been used in clinical medicine as a measure of adrenocortical activity (Roche *et al.*, 1950). Unfortunately, accurate eosinophil counting is difficult, and Godlowski (1951) has demonstrated that heparin in large doses may produce an eosinophilia in spite of injected cortisone or A.C.T.H.

In the present series six of the nine patients who showed the electrolyte and water disturbances described above also showed a reduction of the eosinophil count by 50% in the immediate post-operative period.

Annersten (1949), in measuring the post-operative rise in blood-adrenaline concentration, has observed an immediate post-operative rise in blood sugar. In an earlier paper (Annersten and Norinder, 1946), a raised blood sugar was also observed on the first and second days after operation. In view of the observations of Annersten (1949) and the work of Cannon (1929), this early hyperglycaemia is undoubtedly due to the liberation of excess adrenaline. Although not commented upon, the results of Annersten

(1949) show that the blood adrenaline is falling by the second post-operative day, whereas the high blood-sugar level is maintained. In the present series a considerable rise in blood sugar occurred in four of the seven patients studied, little or no change being observed in the three others.

Urinary 17-Ketosteroid Excretion

The whole 17-ketosteroid excretion in women, and a part of it in men, is derived from cortical androgens (Forbes *et al.*, 1947). The remainder in men, about 4–6 mg. a day, is derived from testicular tissue.

It was early noticed (Fraser *et al.*, 1941) that there was a diminished excretion of 17-ketosteroids in the urine following trauma and surgical operations. However, the same workers (Forbes *et al.*, 1947) demonstrated later that they had missed an early rise in 17-ketosteroid excretion in the first 24 hours after operation. After this, ketosteroid excretion fell to its lowest point about the fourth or fifth day, and by the tenth day regained normal levels. Control patients showed that starvation alone did not cause this rise, and then fall, in excretion. Landau *et al.* (1948) also showed that starvation by itself decreases the total 17-ketosteroid excretion. A sharp rise in the excretion of 17-ketosteroids followed by a fall to below normal levels in 30 patients suffering from haemorrhage, fractures, burns, infection, and operation was shown by Stevenson *et al.* (1944). A similarly elevated 17-ketosteroid excretion was noted by Freeman *et al.* (1944) after severe muscular fatigue. Talbot *et al.* (1945) found evidence of increased urinary excretion of 11-oxysteroid-like substances in active Cushing's syndrome, in adrenal cortical virilism, after burns, and in post-operative patients. Cope *et al.* (1951) observed increased excretion of 11-oxysteroids in acute medical conditions such as diabetic ketosis, congestive cardiac failure, bronchopneumonia, coronary infarction, and status asthmaticus. Forsham *et al.* (1948) demonstrated an increase of both 17-ketosteroids and 11-oxysteroids in the urine after A.C.T.H. therapy. This finding has been confirmed by Sprague *et al.* (1950) in a large series of cases.

In the present series seven of the nine patients showed a large increase in ketosteroid excretion in the first two days after operation, followed by a fall reaching a minimum at the sixth post-operative day. Of the two patients who did not show increased ketosteroid excretion, one showed a slight fall. The other case, excreting 17-ketosteroids before operation at the upper limit of normal, had at that time a very low eosinophil count. After operation 17-ketosteroid excretion fell dramatically, associated with a marked rise in the eosinophil count.

Conclusions

Some evidence has been produced of increased 11-oxysteroid secretion and 17-ketosteroid excretion as a measure of increased adrenocortical activity after operation. This has often been shown in recent years in association with trauma, burns, acute medical conditions, and operation itself. The present study has shown that these changes are also associated with alterations in electrolyte and water balance. Changes of sodium, chloride, and water retention, associated with increased potassium excretion and with exchanges of sodium for potassium within the cells, are very similar to the effects of 11-deoxycorticosterone. Though they may be accounted for by other means, such as local accumulation of fluid and electrolyte in damaged tissues, the fact that they are associated with other evidence of adrenocortical activity suggests that they are themselves linked with such activity. Prunty (1949) has recognized a similar phase of decreased plasma sodium and chloride in acute porphyria. The study of eosinophil counts, uric acid excretion, and neutral reducing steroid excretion indicated an increased adrenal activity during the acute phase of the disease. As Selye has suggested, such a response may occur in a variety of conditions, all in themselves a reflection of injury to the organism.

The retention of sodium chloride and water in the body after operation, in amounts greater than apparent needs, has now become recognized. The diminished urinary excretion of chloride in the first weeks after operation vitiates the urinary chloride estimation as a measure of body chloride requirements. This has been accepted by Marriott (1951). Attempts to replace the apparent chloride deficiency will only lead to water and salt overload. I believe that plasma chloride estimations in the post-operative period are of greater value in estimating body chloride deficiency. Even these determinations, as has been demonstrated in this paper, will give a false low reading.

The importance of potassium in the serum and extracellular fluids has been well recognized ever since the work of Ringer (1883). In recent years great interest has been focused on the loss of potassium in various acute medical and surgical conditions. Brown *et al.* (1944) described low levels of serum potassium in chronic nephritis, associated with muscular weakness and paralysis. Holler (1946) drew attention to a similar low potassium level during the treatment of diabetic coma. It is, however, largely due to the work of Darrow and his associates that clinical potassium deficiency has become widely recognized (Govan and Darrow, 1946; Darrow, 1948; Darrow and Pratt, 1950). As shown by these and other workers, potassium can be lost to the body in gastro-intestinal disorders such as diarrhoea (in children), sprue, intestinal fistulae, prolonged vomiting, and in certain types of diet, such as the Borst diet (Kolff, 1950).

Tarail and Elkinton (1949) have demonstrated that in both normal and potassium-depleted patients the kidney has a limited minimal excretion of potassium, below which minimal level the excretion does not appear to fall. This continued potassium loss, even in the presence of cellular potassium deficiency, they believe to be an important factor in producing further depletion. If, in addition to these other sources of potassium deficiency, the incident of a surgical operation increases the urinary potassium loss, cellular potassium depletion is further increased, and the production of a state of clinical potassium deficiency is hastened. The fact that the rapid mobilization of cellular potassium after an operation is often associated with a rise in serum potassium concentration makes the recognition of cellular depletion all the more difficult. I have seen several patients with a cellular potassium deficiency in which the serum potassium, though falling from a concentration greater than normal, was still within the normal range when electrocardiographic evidence of cellular potassium deficiency was detectable.

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ANNULAR PANCREAS

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The commonest developmental abnormalities of the pancreas concern the ductal systems. Accessory pancreatic tissue—isolated masses separate from the main gland—occurs not infrequently in the stomach or duodenum, but may be found in most of the abdominal viscera. Other anomalies are pancreas divisum (Hyrtl) consisting of two separately functioning glands; bifid tail of the pancreas; and annular pancreas in which a band of pancreatic tissue encircles the duodenum, usually in its second part. Cysts and fibrocystic disease may occur.

In 1933 McNaught was able to find descriptions of only 40 cases of annular pancreas in the literature, the first three referring to the condition in birds, in which it is apparently a normal finding (Ravitch and Woods, 1950). In June, 1952, the total number of cases recorded was at least 75, and it is significant to note that 20 of these have been recorded since the end of 1949, indicating a higher actual incidence than the statistics show. In the absence of obstruction, cases may easily be overlooked either at operation or at necropsy.

A further case has recently been brought to light during an operation for chronic duodenal ulcer by one of us (N. C. T.).

Case Report

A male clerk aged 30 was admitted on October 13, 1951, with a history of two and a half years' epigastric pain two hours after meals, relieved by food, rest, and alkalis. There had been periods of freedom of up to nine months. He had no vomiting, but had lost 28 lb. (12.7 kg.) in weight since the onset. After investigation elsewhere he was told that a duodenal ulcer was present. The only abnormality detected was a gastric succussion splash. A gruel fractional test meal showed a high acid curve rising to 65 ml. N/10 free HCl at one hour.

A barium-meal examination disclosed a spastic deformed duodenal cap with folds radiating from an ulcer scar. There was no gross obstructive lesion of the second part of the duodenum. In view of his relapse despite more than one good course of medical treatment, he was operated upon on October 16. The presence of an anterior chronic duodenal ulcer was confirmed. The rest of the viscera appeared normal, except that, about 2–3 cm. below the junction of the first and second parts of the duodenum, the organ was encircled by pancreatic tissue of healthy appearance and texture, the abnormal part being a band about 1–2 cm. in diameter (see illustration). A subhiatal vagotomy and Heineke – Mikulicz pyloroplasty was then carried out. During the pyloroplasty opportunity was taken to feel the duodenum from within its lumen, and there appeared to be no appreciable constriction. The patient made an uncomplicated recovery from this operation, and an insulin test meal 17 days later showed a much lower acidity and no secretory response to the insulin.

Diagram showing band of pancreatic tissue encircling the duodenum.

Nine months after operation the patient was symptom-free, and a further barium-meal examination showed no delay in emptying of the stomach and no evidence of constriction of the duodenum.

Discussion

Aetiology.—The condition affected males in 50 out of the 64 cases in which the sex was recorded. Various theories have been advanced concerning the embryological origin of the ring—for example, persistence of the left half of the ventral anlage of the pancreas which ordinarily atrophies, fixation of the ventral bud of the pancreas to the duodenum before rotation of the gut, or a smooth spread round the duodenum as is said to occur in birds. Other congenital abnormalities have been found associated with the annular pancreas in some 20 cases, the most frequent being malrotation of the abdominal viscera.

Symptomatology.—Patients with annular pancreas may present at any age with symptoms due to the condition, or the condition may be symptomless. The youngest recorded case was in a 16-mm. embryo (Weissberg, 1935), while two cases were operated upon at the age of 74 (Smetana, 1928; Custer and Waugh, 1944). Thirty-seven cases had symptoms due to the annulus. Most of the nine presenting in the first decade appeared shortly after birth, with symptoms of high intestinal obstruction or with jaundice probably due to compression of the common bile duct. If symptoms have not developed by this time it would seem reasonable to suppose that the patient has a good chance of remaining symptom-free throughout life. A study of the literature suggests that this is not the case. Adults usually present with high intestinal obstruction, with symptoms suggesting peptic ulceration, or, less commonly, with acute haemorrhagic pancreatitis. In the first there may be rapidly progressive or recurring episodes of obstruction. This sometimes results from pancreatitis of the annulus, but this is not a constant finding in those specimens which have been sectioned. Those patients with a history suggesting peptic

ulceration may indeed have peptic ulcers as in the present case. Eight additional cases associated with peptic ulcers have been recorded (gastric 3, duodenal 5). Four further patients had a history of haematemesis or melaena. Acute haemorrhagic pancreatitis is a rare presentation, but has been recorded.

Differential Diagnosis.—The diagnosis has been suggested pre-operatively in eight cases. It will be considered only when there is a sufficient degree of deformity or obstruction to be shown by a barium-meal examination. Other possibilities to consider include congenital bands associated with malrotation, tumours of the pancreas or sphincter of Oddi, ulcer and rarely primary or secondary cancer of the second part of the duodenum, and pressure by enlarged glands from without.

Treatment.—If surgical treatment is indicated the choice of procedure lies between section of the ring and some form of by-pass operation. The former carries some risk of fistula formation, and so the site of division should be protected by a drain to the exterior. This may be combined with longitudinal division and transverse suturing of the duodenum, the suturing being made in such a way as to drain the cut ends of the pancreatic annulus into the lumen. This duodenoplasty overcomes any intrinsic duodenal narrowing and the possibility of recurrent obstruction. Partial gastrectomy is a somewhat severe method of dealing with an annular pancreas unassociated with other gastro-duodenal disease. Gastro-jejunostomy introduces an undoubted risk of stomal ulceration, and, if feasible, duodeno-jejunostomy would be preferable.

Summary

A case of annular pancreas is reported. The finding was an incidental one at operation for chronic duodenal ulcer. No obstruction of the duodenum was produced, and the presence of the condition did not affect the operative treatment of the ulcer.

We are indebted to Drs. R. Quilliam and A. Jenkins for the radiological reports and to Mrs. Mace for the picture.

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SLIDING HERNIAS THROUGH THE OESOPHAGEAL HIATUS

BY

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[WITH SPECIAL PLATE]

The anatomical abnormality of hernia through the diaphragm was first referred to in 1570 by Ambroise Paré, who noticed the condition at a post-mortem examination and attributed it to trauma. Fothergyll (1746) described a congenital variety. The first diagnosis during life was made by Newman (1888), who also performed the first operation for its cure. Akerlund (1933) made a careful study of all types of diaphragmatic hernia, and his classification has formed the basis for much subsequent work. In recent years the frequency of diaphragmatic or hiatus hernia has been fully recognized, and there are many publications available on the subject.

*Working as a scholar from Spain under the British Council.

The present paper deals with only one variety of hiatus hernia, the so-called "sliding hernia," which is the commonest of all, and which has been excellently described by Allison (1951). A sliding hiatal hernia is chiefly encountered in adults who are past middle age, and must therefore be regarded as quite distinct from a congenital defect. In considering its aetiology, two matters appear to be of prime importance: (1) the exact anatomical status of the so-called "cardia," or junction between oesophagus and stomach; and (2) the part played, structural and physiological, by the terminal part of the oesophagus as it passes through the diaphragm.

The So-called "Cardia"

In a study of the cardia, clarity in certain anatomical points is essential: (*a*) the nature of the boundary between the oesophageal and gastric mucous membranes; (*b*) the normal relationship of the boundary of the two mucous membranes to the exit through the diaphragm; (*c*) the question of a real anatomical sphincter at or close to the boundary; and (*d*) the site of the change in shape from tubular (oesophagus) to saccular form (stomach). These points can be made out only by careful microscopical examination of the whole zone in specimens removed in the post-mortem room and fixed by most careful technique to preserve and identify exact relationships. Macroscopic methods such as changes in colour, difference of shape, and even *x*-ray films taken during life are not exact enough, and may indeed be very misleading. Oesophageal structure is clearly identified microscopically by its stratified squamous epithelium, and stomach structure by its characteristic mucous membrane. Microscopical investigation clearly shows that the junction of the two mucous membranes is not a ring, but follows an irregular curve. Moreover, although the junction of the two mucous membranes is clean-cut, it is not unusual to find areas of gastric mucosal glands lying below the stratified oesophageal lining membrane. The opposite, however, does not occur.

In the photomicrograph (see Plate) this transition is clearly seen, and the two muscular layers are also well demonstrated. The point should also be noted, as has been found microscopically, that the diaphragmatic muscle does not clasp the oesophagus at a fixed level or point—there is an agglomeration of muscle fibres and loose fibrous tissue which allows the oesophagus to slide up and down for a short distance, this being essential for the normal respiratory movement of the diaphragm. In what may here be termed normal cases, accurate marking showed that the level of the diaphragmatic insertion and the junction of the two mucosae never coincided. Oesophageal stratified epithelium was always found at this level, indicating that the normal junction is below the diaphragm and just above the point where the saccular expansion of the stomach begins. This explains the curious observation that carcinoma of the fornix of the stomach extends to the cardia. That is to say, it invades the lowest tubular portion, with resultant incompetence or stenosis. No observation has been made of a carcinoma of the oesophagus (properly called) subsequently invading the fornix. It would seem, therefore, that a tumour always infiltrates the same structure and the change of lining membrane constitutes a barrier. A gastric carcinoma which invades the lowest tubular part invades its own structure, not the oesophagus.

Terminal Part of the Oesophagus

No evidence was found microscopically of any true muscular sphincter at the lower end of the oesophagus. As has been stated, the joining line between the two mucosae is an irregular curve and never a ring, and a ring form would almost be required for a true muscular sphincter. Thus, as Barrett (1952) has pointed out, the cardia and sphincter mechanism are not synonymous.

Lendrum (1937), in a careful anatomical study of the cardia in 150 cases, also concluded that no ring-shaped muscular reinforcement was present. No muscular thickening was found in the present investigation. Although there is thus no obvious and clearly defined muscular sphincter, this does not exclude some potential sphincter mechanism of a kind less positive than, for instance, the pylorus of the stomach. I believe that a segment of the oesophagus, extending for about 1 in. (2.5 cm.) above the stomach, may act as a sphincter. This view is supported by our knowledge of cardiospasm (first described by Purton in 1821), in which there is no ring of closure but a narrowing over about 1 in. (2.5 cm.) of the tube. This, indeed, is the basis of Heller's operation, with an incision in the oesophagus about 1 in. (2.5 cm.) in length.

There are many other views concerning a potential sphincter mechanism between oesophagus and stomach, and the action is often nowadays referred to as resembling a "pinch-cock"—generally adequate, but easily overcome to permit regurgitation. Lendrum (1937) has even suggested that muscular fasciculae in the stomach wall may on contraction contribute to a sphincter action, but this view has not received support. As Alvarez (1939) points out, the diaphragm will act as a sphincter when the intra-abdominal pressure is very high. Its action cannot be important, however, since patients with patency of the hiatus or hiatus hernia do not have continuous regurgitation.

The sphincter action, such as it is, is clearly under nervous control by Auerbach's plexus and by the sympathetic and parasympathetic systems.

Patency of the Oesophageal Hiatus

The question of patency of the hiatus was investigated in the post-mortem room of the Western Infirmary in 50 consecutive necropsies, in adults between the ages of 31 and 78 years. A finger—sometimes two fingers—was inserted into the hiatal region from the abdomen, and cases in which one or two fingers could be inserted for a distance of 2–3 cm. are described as *positive*, and the others as *negative* (see Table). Cases in which an operation had been performed in the area of the stomach or adjacent parts were excluded. The Table shows that in 13 of the 50 cases examined (26%) the hiatus was to some extent open so that herniation above the diaphragm would easily be possible. It is not thought that the laxity of tissues in the cadaver would account for this, in view of the numerous negative results. It must be remembered that three important structures pass through the diaphragm close to one another—the aorta, the inferior vena cava, and the oesophagus. The first two openings are always firmly closed, so that herniation is virtually impossible; it is only the oesophageal opening which is not. The oesophageal passage is elliptical in shape, to allow for considerable distension of the oesophageal tube as food passes through it, and the extra space is filled up by loose fibrous tissues. Here is obviously a weak spot in the separation of the abdominal and thoracic cavities.

Summary of 50 Consecutive Necropsies

Case No.	Age	Sex		Case No.	Age	Sex	
1	40	F	+	26	61	M	+
2	63	F	−	27	61	F	−
3	45	M	−	28	64	F	−
4	51	M	−	29	52	M	−
5	78	M	+	30	52	F	−
6	60	M	−	31	72	M	−
7	52	M	−	32	72	M	+
8	65	M	−	33	47	F	−
9	65	F	−	34	62	F	+
10	66	F	+	35	45	M	−
11	57	M	−	36	35	F	−
12	77	M	−	37	61	F	−
13	59	M	−	38	55	F	+
14	55	M	−	39	54	M	−
15	55	F	−	40	31	M	−
16	37	F	−	41	78	M	−
17	69	M	−	42	75	M	+
18	62	M	+	43	64	M	−
19	75	M	+	44	55	M	−
20	60	M	−	45	59	M	−
21	68	F	−	46	49	F	−
22	60	M	+	47	53	M	+
23	54	F	−	48	73	M	−
24	73	M	−	49	35	F	−
25	73	F	−	50	64	M	+

In the series of cases referred to, patency was found only in the anterior and left lateral part of the hiatus, and never in the posterior and right lateral part, although loose fibrous tissue surrounds the oesophagus on every side. The reason is clearly because (Gray, 1926) only the anterior and left side is covered by peritoneum on the abdominal side, and it is only in such a place that a sliding herniation can arise.

X-ray Findings Compared with Post-mortem Findings

Johnstone (1952) and Pickard (1952) have both reported a surprising number of hiatus hernias during routine *x*-ray examination of the gastro-intestinal tract, but only when the patient is placed in the "head-down and feet-up position," as first recommended by Soresi in 1919. Pickard's percentage in such *x*-ray examinations was 11%, in contrast with 26% in my series of post-mortem observations. There must be some reason for this discrepancy, and it is suggested that it is only when patency is well marked that the hernia appears during *x*-ray examination.

Summary

An investigation has been made of various points concerning the aetiology of the "sliding" type of hiatus hernia.

It was evident that before reaching any conclusion a careful study of the so-called "cardia" was essential—that is to say, of the junction between oesophagus and stomach and of the passage of the oesophagus through the diaphragm.

The results of macroscopic and microscopical examinations of this area are given in detail.

There is no clearly defined anatomical sphincter at the lower end of the oesophagus, and the squamous lining ends in an irregular curve and not in a ring. This, however, does not exclude a broad but weak contractile mechanism in the lower part of the oesophagus.

In an unselected series of adults carefully examined in the post-mortem room, patency of the hiatus was detected in 26%. This finding has been interpreted as evidence of potential hiatus hernia. The patency was always found at the anterior and left lateral part of the passage of the oesophagus through the diaphragm.

This investigation was carried out during the tenure of a British Council Scholarship. I am indebted to Professor Sir John McNee for help and guidance, and also to Professor D. F. Cappell and his staff for many facilities in the department of pathology at the Western Infirmary, Glasgow.

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A recent survey by the National Agricultural Advisory Service has shown that washed eggs are specially likely to go bad after storage. This is an important factor, since the survey also revealed that an average of one egg in three is soiled in the nest. Research into this problem is being carried out by the Food Investigation Organization.

OSTEOID OSTEOMA

BY

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[WITH SPECIAL PLATE]

Osteoid osteoma is a benign tumour of bone. Since its first description (Jaffe, 1935) many cases have been reported in the American literature, but there are singularly few publications on this subject in the British literature, and only one case report (Vaughan-Jackson, 1950). This would suggest that osteoid osteoma is a rarity in the British Isles, whereas it is more likely that the condition often passes unrecognized. This would seem to be of no great consequence, because the lesion is benign and if untreated probably heals spontaneously after many years (Sherman, 1947b ; Moberg, 1951). On the other hand, amongst the abundant case reports from the United States and Canada are some of patients who underwent unnecessarily radical treatment such as amputation and resection because of a mistaken diagnosis of malignancy or tuberculosis. The recognition of osteoid osteoma is therefore of importance. The following case is reported as a typical example of the condition.

Case Report

A girl aged 12 was referred to the orthopaedic department of Alder Hey Children's Hospital in September, 1950, suffering from pain in the tip of her right second toe of two years' standing. She did not recall having injured the toe. The pain was slight and intermittent at first, but during the past few months it had been more severe, especially at night.

On examination there was a bulbous, tender soft-tissue swelling of the terminal phalanx. The toe-nail was slightly deformed. A radiograph showed a small, rounded, well-defined, translucent area in the tip of the terminal phalanx containing what appeared to be a minute sequestrum. An inflammatory lesion was suspected, and amputation of the terminal phalanx was carried out in November, 1950. The wound healed by first intention and all symptoms subsided. When the patient was seen in March, 1952, the stump was found to be satisfactory and there were no complaints.

Pathological Report.—Gross Appearances: The terminal phalanx of a toe disarticulated at the joint. On longitudinal section, at the tip of the phalanx, there is a well-circumscribed yellowish-grey finely trabeculated lesion 3 mm. in diameter. At the distal end the normal cortex cannot be distinguished from the lesion. It is moderately firm in consistency and does not exude pus on compression (see illustration, Special Plate). *Microscopical Examination:* "The proximal portion of the phalanx shows a perfectly normal picture. As one progresses distally, the cortex beneath the nail shows well-marked narrowing and osteoclastic absorption. In some small areas it has been destroyed and replaced by the expanding central lesion. The distal end and a little of the undersurface of the phalanx show a similar picture. The lesion itself consists of irregularly arranged trabeculae of osteoid in which there is early calcification. The intervening spaces are filled with a vascular matrix, consisting of large numbers of cells with fibrillary processes, which at the edges of the spaces are arranged as rows of active osteoblasts. In some areas previously formed and calcified trabeculae are being destroyed by osteoclasts. Occasionally there lies between the lesion and the surrounding bone a fairly narrow zone of the vascular matrix mentioned above, devoid of trabeculae of osteoid or bone. The lesion is a typical osteoid osteoma. There is no histological evidence of infection, and cultures from the lesion were sterile."

Discussion

In retrospect the case appears to be typical of the condition, and the diagnosis should have been suspected on clinical and radiological grounds. An almost identical case has been reported (Pritchard and McKay, 1948) as occurring in the terminal phalanx of the second toe of a boy of 13 in whom the diagnosis of tuberculosis was made and the phalanx was amputated.

Osteoid osteoma occurs in adolescents and young adults and is rare after the age of 30. It is twice as common in males as in females. It is a single lesion, more common in the bones of the lower limbs than elsewhere.

Characteristic clinical features are the well-localized and persistent pain, often worse at night, and the local tenderness. Swelling is a less constant sign, and is confined to the soft tissues if the lesion is in the spongiosa of a small bone. Should the tumour be situated in or near the cortex of a long bone a bony thickening due to reactive periosteal new-bone formation may be present. Other signs of inflammation, local or general, are consistently absent. If the lesion is situated in the vicinity of a joint it may cause a non-specific synovitis (Sherman, 1947a).

Radiologically, there is a well-defined rounded translucent area, seldom larger than 2 cm. in diameter. In the early stages the contained tumour nodule is radio-translucent, but later the osteoid material becomes calcified and looks like a sequestrum in the *x*-ray film. Often there is a narrow ring of increased density surrounding the lesion.

The tumour may be situated either within the cancellous bone or in the cortex of a long bone (subperiosteal or subcortical). In the latter situation it gives rise to a marked periosteal reaction, and dense subperiosteal bone is deposited which may obscure the translucent lesion. In this particular situation it is difficult to differentiate it from a chronic infective lesion—the chronic subperiosteal abscess (Brailsford, 1942). Only histological and bacteriological examination will decide whether it is an osteoid osteoma or an inflammatory process.

Treatment by local excision or curettage has been found satisfactory by all authors and no recurrence has been reported.

Summary

A case of osteoid osteoma is reported. The clinical, radiological, and pathological features are described.

I wish to thank Mr. F. C. Dwyer for permitting me to publish this case, and am indebted to Dr. E. G. Hall for his detailed pathological report.

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The London County Council has a scheme whereby medical officers employed by the council at maternity and child welfare centres are exchanged with paediatric registrars at the following hospitals: St. George's Hospital, the Hospital for Sick Children, Westminster Children's Hospital, King's College Hospital, Guy's Hospital, Paddington Green Children's Hospital, and the Queen Elizabeth Hospital for Children. In addition there is an exchange system with St. James's Hospital, Balham, and a paediatrician from St. Thomas's Hospital goes to North Lambeth Babies' Care Welfare Centre to take weekly child welfare sessions.

Medical Memoranda

Haemolytic Disease in a First-born Infant

Haemolytic disease is rare in first-born infants; the stimulus of a second rhesus-positive foetus is apparently nearly always required before the maternal antibody is produced in sufficient potency to affect the infant. When haemolytic disease has been observed in a first-born it has usually been explained by previous sensitization to the Rh antigen by a transfusion or injection of Rh-positive blood or a pregnancy which ended in an early abortion. The following case is of interest because it seems likely that there was no sensitization before the onset of the first pregnancy, which ended with the birth of an infant suffering from haemolytic disease.

CASE REPORT

A woman aged 27, who had been married for three years, was delivered of an apparently normal female infant weighing 7 lb. (3.2 kg.). A few hours after birth slight jaundice was noticed, and the next day the skin was a deep golden yellow.

On admission to hospital some 36 hours after birth, the infant was still deeply jaundiced, with slight enlargement of the spleen; otherwise it appeared perfectly normal. The laboratory findings were typical of haemolytic disease. The mother was Group A rhesus-negative and her serum contained strong saline and albumin rhesus antibodies. The infant was Group O rhesus-positive. The direct Coombs test was strongly positive. The serum bilirubin was 20 mg. per 100 ml.

The infant's haemoglobin fell steadily from 80% (11.8 g.%) on admission to 58% (8.6 g.%) on the ninth day, when, after a transfusion of 180 ml. of blood, it rose to 102%. There was a further slow fall in haemoglobin, but no further transfusion was needed.

The mother was an intelligent woman, a laboratory worker, who understood the significance of her evidence. She had previously been a blood donor, but neither she nor her parents could recall any occasion when she had been injected with blood or serum: she had, in fact, always been in good health. Furthermore, she had never had any abortions; whilst her menstrual cycle had always been irregular (4–7/24–35), the longest period of amenorrhoea prior to becoming pregnant was 39 days, ending with a menstrual loss no heavier than usual.

COMMENT

Mollison (1948) states that antibody formation may begin as early as the twelfth week of pregnancy, but it is not usually until the second or later pregnancy that haemolytic disease appears.

It is well established that the injection of rhesus-positive blood into a rhesus-negative subject acts as a most powerful stimulus to the production of antibodies, so that a woman's first-born child may suffer from haemolytic disease.

It is, however, not so well proved that, in the absence of previous sensitization, the first-born may be affected: when Levine and Waller (1946) reported 28 cases of haemolytic disease affecting the first-born, they found that 19 of the mothers gave histories of a previous transfusion or injection of blood; of the other nine cases the authors concluded that the possibility of previous sensitization could not be excluded, as it used to be a widespread practice—that is, in the U.S.A.—to inject a few millilitres of blood at birth to prevent haemolytic disease. Cappell (1946) mentioned four families in which the first-born were affected; and Spalding (1947) recorded a first pregnancy resulting in a hydrops foetalis: the mother had rhesus antibodies and there was no history of previous sensitization.

Few other cases have been published, although the incidence may well be greater than this fact suggests.

My thanks are due to Dr. J. J. Tillie for permission to publish this case and for advice, and to Dr. P. N. Coleman for laboratory reports.

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Subcostal Pain Following Controlled Respiration

An unsolicited complaint of subcostal aching during the first post-operative day after controlled respiration, especially with succinylcholine relaxation, seems to be a common complication.

The cases seen so far have been confined to females aged 20 to 65 years, both athletic and sedentary. Thus in a series of 40 consecutive dental operations (12 males, 28 females) there was no complaint from the male group, but subcostal pain was noted in six (21.4%) of the females (see Table).

Agent	Male		Female	
	No. of Cases	Subcostal Pain	No. of Cases	Subcostal Pain
Succinylcholine	7	0	12	4
Gallamine triethiodide ..	1	0	4	1
No relaxant (thiopentone, pethidine)	4	0	12	1
Total cases (40) ..	12	0	28	6

The site of operation in these cases—for example, dental procedures, excision of glands of the neck, etc.—is remote from the abdomen: the pain following operative trauma in the latter presumably overshadows, or is associated with, post-operative subcostal ache. Most of the patients have required passive inflation for short periods only (5 to 10 minutes) after intubation.

This subcostal pain first appears soon after consciousness is regained, and persists for 24 to 48 hours. It varies in severity and distribution from that of a minor anterior subcostal discomfort to a severe ache encircling the costal margin and extending to the back. Forced respiration and movements involving the abdominal musculature, such as sitting up or turning, cause acute discomfort. The disturbing feature is that the patient, at the time, usually complains more of the discomfort subcostally than of the pain at the site of operation. (A young lady who awakens expecting an aching jaw, only to find something worse at her midriff, rightly asks for an explanation.)

This complication has only occasionally been seen when relaxation has been produced with other agents, and seems to be more commonly associated with the greater degree of relaxation obtained by succinylcholine. Thus, with this agent, passive inflation can presumably cause a greater degree of stretch of the respiratory musculature with minimal resistance. I do not think that the transient excitation preceding paralysis with succinylcholine is concerned in the mechanism.

That the complaint has been confined to females is probably accounted for by their inherent thoracic type of respiration, passive inflation with full relaxation causing an unaccustomed stretching of the muscle fibres of the diaphragm. As one intelligent patient put it, "My diaphragm feels as though it has just played its first game of squash for the season."

An awareness of this complication might indicate the need for less vigorous inflation during the period of complete relaxation, which should result in a decrease in the incidence of post-operative subcostal pain.

Acknowledgments are due to my colleagues at the Westminster Hospital for allowing access to their records and to Dr. G. Organe and Dr. C. F. Scurr for their helpful criticism.

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Reviews

ATLAS OF INFECTIOUS DISEASES

World Atlas of Epidemic Diseases. Part I. Edited by Professor Ernst Rodenwaldt. (Pp. 126; 52 maps. No price given.) Sponsored by the Bureau of Medicine and Surgery, Navy Department, Washington, 25, D.C. Hamburg: Falk-Verlag. 1952.

Epidemiologists are continually faced with the problem how to present data about incidence of infective diseases geographically whilst at the same time taking account of the degree of completeness of records, seasonal variation, and year-to-year variation or long-term trend. When reporting on events in a single country in a single year the problem is comparatively simple, but to present in a nutshell a world-wide picture of endemicity in relation to climate, geography, migration of population, and advance of civilizing influences, of the spread of epidemics in space and of seasonal swing in relation to latitude, is far from simple. No more ambitious attempt to accomplish this has been made than in the publication of the *World Atlas of Epidemic Diseases.*

The atlas, designed to appear in two parts, is edited by Dr. Ernst Rodenwaldt with numerous collaborators in Germany, under the sponsorship of the Bureau of Medicine and Surgery of the U.S. Navy Department. Part I, now available, consists of 40 large folding maps dealing with 17 infectious diseases and the distribution of rainfall, temperature, and population in Europe, a series of 12 basic maps of different regions of the world, and 118 pages of textual comment in German and English. The whole is bound together in a massive cover permitting removal of the maps.

The maps are beautifully reproduced and coloured according to altitude, the epidemiological data being superimposed on them by various diagrammatic devices. Seasonal swing, for example, is depicted by a circle containing a red sector which indicates by its position the month when incidence is greatest and by the length of its radius the relative frequency during that month compared with the average month. Comparative incidence in a specified period of years is depicted by cross-hatching. Most of the maps in this part are limited to Europe and the Near East, but world maps are included for typhoid, paratyphoid, cholera in 1863–8, and leptospirosis. The climatological maps of Europe and the Near East are a most useful feature, including as they do average rainfall, January temperature, July temperature, annual temperature, and range.

It is not possible in a short review to comment on the textual matter. The defects of the basic data available from many of the countries are well known to epidemiologists and are admitted by the editors. The cost of production must have been very considerable, and it is to be hoped that the atlas, which measures 19 by 15 in. and weighs over 12 lb., will not spend its life on library shelves, for its usefulness in teaching is enhanced by the facility with which individual maps can be taken out for demonstration purposes.

PERCY STOCKS.

RADIOGRAPHY OF SKULL AND BRAIN

The Skull and Brain Roentgenologically Considered. By C. Wadsworth Schwartz, Ph.B., M.D., F.A.C.R., and Lois Cowan Collins, B.S., M.D. (Pp. 386; 335 figures. £3 17s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1952.

That plain radiographs are essential in the diagnosis of tumours and many other lesions of the skull and brain has been recognized for nearly half a century now. What seems to be much less obvious is that plain radiographs are usually only the first step in the radiological investigation. More than one textbook on the radiology of the head has been published in recent years in the English language confining its attention almost entirely to plain radiographs. The present work is no exception. The title would appear to imply that the reader will find the answers to the diagnosis both of skull and brain tumours and of tumour-like masses. In this he will be disappointed, particularly so far as the brain is concerned.

Although a magnificent museum collection of lesions demonstrable by plain radiography is displayed in over three hundred radiographs, the point is not made clear that in only a small minority of cases can *x* rays, without the aid of contrast substances, reveal the site and pathology of an intracranial mass sufficiently accurately for a surgeon to approach the lesion with confidence.

The authors first describe the normal appearances and variants seen in the skull. Chapters on congenital anomalies and fractures follow. The remaining two-thirds of the book is given to neoplasms and miscellaneous diseases. The student or uncritical reader will derive a quite false impression of the relative commonness of lesions seen in neuroradiology. For example, nearly twice as much space is given to tumours of the skull itself, relatively rare lesions, as to gliomas—quite the commonest brain tumours. Air studies and angiography would appear to play a small part in the diagnosis of the latter, in spite of the well-known fact (mentioned by the authors) that only about 13% of gliomas calcify. The chapter on acoustic tumours is very poor. The diagnostic value of plain radiographs in cases of acoustic tumour is not made clear, but reference to Chart II, some ninety pages earlier in the book, gives 15% as the figure for widening of the internal auditory meatus visible on plain radiographs. Over 70% is the usually accepted figure.

Clinicians and morbid anatomists will also have faults to find. For example, on page 204 the authors state: "Tumours of the acoustic nerve, as a rule, develop in patients during their third decade. . . ." Of colloid cysts they say: "It is extremely rare for one of these cysts to contain sufficient calcium to be seen in the roentgenogram"; then again, "The larger cysts may block the aqueduct or posterior part of the third ventricle." The reviewer is unaware of any calcified colloid cysts in the literature. Moreover, it is generally accepted that these cysts are derived from the paraphysis, a structure which lies some 4 cm. away from the aqueduct.

The many radiographic reproductions are of excellent quality. However, if a second printing is made it is hoped that Fig. 194, which reproduces the optic foramina upside down, will be correctly orientated. The interpretation of radiographs of the optic foramina is not always easy even when viewed the right way up.

J. W. D. BULL.

CAUSALITY IN THE MIND

Reason and Unreason in Psychological Medicine. By E. B. Strauss, M.A., D.M., F.R.C.P. Foreword by Sir Russell Brain, P.R.C.P. (Pp. 55. 8s. 6d.) London: H. K. Lewis. 1953.

The principle of causality—that is, the operation or relation of cause and effect—is often assumed to be valid when in fact it lacks adequate philosophic support. Psychological medicine, following in the wake of general medicine, has fallen into unreason, according to Strauss, because of its whole-hearted acceptance of causality. This has led to a pseudo-scientific attitude of mind towards aetiology and treatment. "Diseases" are regarded as entities with causes which, if known, can be removed by treatment. The urge to find a simple efficient cause of disorders, to the exclusion of other relevant agents, has produced ineffective forms of treatment.

The title of this book is that selected by Dr. Strauss for the Croonian Lectures for 1952. These and a third lecture, "Quo Vadimus?" form the book. The theme is a scrutiny of the principle of causality as it bears on the theory and practice of medicine, and in particular psychological medicine. The main force of the argument, or rather indictment,

falls on psycho-analysis. Psycho-analysis as a body of knowledge and as a therapeutic system rests on the assumption that there is an efficient cause for all neuroses and faulty adaptations to life—namely, failure to solve the Oedipus complex. The conclusions of psycho-analysis are grouped round this complex, the most significant finding of Freud and his disciples. Causality, Strauss contends, is not so plain as this. Aetiology is multiple, a network rather than a simple cause-effect relationship. His thesis, supported by cogent reasoning, is an important contribution and should be of special interest to psycho-analysts, who "inhabit a little world of their own that is apt to be quite out of touch with systems of thought which are foreign to them."

The principle of multiple aetiology, so strongly advocated, has much to commend it. But it is not the final answer. Strauss makes no reference to the principle of synchronicity which has figured in recent work in analytical psychology. This omission might well be remedied should an enlarged version of this volume be called for.

E. A. BENNET.

STERILITY

Sterility: Its Cause and Its Treatment. Part I: The Infertile Female. Part II: The Infertile Male. By J. Jay Rommer, A.B., Ph.G., M.D., A.I.C.S. (Pp. 424; 152 figures. £4 10s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1952.

The author claims that this book crystallizes all existing thinking and knowledge on the cause and treatment of sterility, and it certainly covers a wide field. But the claims cannot be upheld, for the bibliography is far from up to date, and, perhaps more important still, many old and now outmoded ideas are put forward quite uncritically. There are also some muddled and even erroneous descriptions, such as those of the gonadotrophins and the alleged inflow of seminal fluid through the cervical canal.

Long lists of causes of sterility "culled from the literature, both American and foreign," even with percentage incidences (of uncertain derivation) have a strictly limited value. The chapter on anatomy and embryology scarcely warrants a place and is most oddly sandwiched between "Physiology of Coitus" and "Psychic Trauma and Fertility." It is not clear why two photomicrographs of testis showing normal spermatogenesis should be included, and still less why crystals of testosterone should deserve an illustration occupying two-thirds of a page. The aspiration of the epididymis and testis is advocated as a method of examining for spermatozoa. It is admitted that this may be quite fallacious, and may cause severe pain, so why not condemn it outright? Instead two large illustrations of the technique are shown. The most impressive aspect of the book is its general format, the standard of which is very high; but so is the price at 90s.

G. I. M. SWYER.

HAMEY THE YOUNGER

The Stranger's Son. By John J. Keevil. (Pp. 230. £1 1s.) London: Geoffrey Bles. 1953.

"Let us now praise famous men . . . but some there are that have no memorial." Baldwin Hamey the younger (1600–76) does not belong to either class. He is not famous save among those few interested in the history of the Royal College of Physicians of London, where alone he has some small memorial. But the telling of even the meanest life—and Hamey's was very far from mean—if rightly told, may be an entrancing human document. For such telling Dr. Keevil has all the essentials. He is an industrious historian, well trained though self-trained; he chooses subjects for whom he has special understanding; and he has that narrative skill that conceals the teller in the tale. Some literary Mephisto has beguiled him into putting some of his best points into notes, but, when free of his demon, Dr. Keevil is a writer of high distinction.

The book is a sequel to Dr. Keevil's *Hamey the Stranger* which we reviewed in the *Journal* of April 11 (p. 821). The younger Hamey was most happily born and taught, for his armour was his honest thought and simple truth his utmost skill. He inherited a sound but highly conservative medical tradition and practice in London, where he was born. He drew on the advantages of education at Leyden and Oxford and the moral support of the Royal College of Physicians, to which he was devoted and of which he was a great benefactor. He was happily married to a charming and able woman. His professional integrity was spotless, and by his practice he amassed a fortune, which he disposed of most generously during his lifetime. He was ever a patron of poor scholars, and he died respected and loved. His life course crosses that of many great men of the time, including Harvey. He was to the end a cultivator, along the most rigid lines, of the classical languages, just when the Royal Society had decided to abandon them for scientific and medical discourse. Although he was a capable, industrious, and well-trained anatomist, his conservatism caused him to miss entirely the whole movement—then called "the new philosophy" but which we call "science"—active at his very doors. None of these things suggest a very eventful life, but the events of life are within and not without.

With his sympathy, his power of insight, and his skilful use of background, Dr. Keevil has produced a most readable volume which pictures practice in London 300 years ago with a vividness to which there are very few parallels.

CHARLES SINGER.

CASCADE STOMACH

L'Estomac en Cascade. By Dr. Jean Roussel. (Pp. 132; 60 figures. No price.) Paris: Masson et Cie. 1952.

This monograph is based on the clinical and radiological study of eight examples of cascade stomach in men. Each example is illustrated by retouched radiographs accompanied by explanatory diagrams. The author considers the possible cause of the condition in great detail and is satisfied that contraction of the various gastro-epiploic folds due to "perigastritis" is the essential lesion. This contraction, he believes, may result from organization in folds initially shortened by spasm due to splanchnic irritation. In one case he attributes the cascade appearance to reflex irritation from a mildly inflamed appendix. Yet as common causes of perigastritis he lists alcoholism, arteriosclerosis, chronic peritonitis, and syphilitic and tuberculous peritonitis, in none of which does spasm, such as he envisages, appear likely to occur. He rejects the opinion that gaseous distension of the colon is in any way connected with it.

Roussel associates with the radiological appearances two major clinical symptoms—epigastric fullness and loss of weight. He finds that the fullness is often accompanied by eructations, palpitation, regurgitation, and even vomiting. The loss of weight, which may be rapid and considerable, he attributes to protective anorexia, the patient refusing to eat because he feels more comfortable with an empty stomach.

The treatment advocated ranges from medical restrictions of diet through splanchnic blocks, operative adhesion section to gastro-gastrostomy with anastomosis between the upper and lower pouches of the cascade stomach. A section is also devoted to rather abstract consideration of the mechanism of production of the radiological appearances in terms of forces and tone.

The author's conclusions are too often based on abstract theories and on inductive reasoning to deserve the consideration that might otherwise have been their due. Cascade stomach may at times be accompanied by symptoms, and this deserves recognition and further study. The best service the author has done is to stimulate interest in the condition.

F. PYGOTT.

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PREMENSTRUAL TENSION

Women are slow to complain about what they regard as woman's lot. The cramps of dysmenorrhoea, the sorrows of dyspareunia, the pangs of childbirth, and the discomforts of the climacteric may all be suffered, if not in silence, at least without complaint to the doctor. To these more notable disabilities must be added the premenstrual tension state, a syndrome thus named by Frank in 1931[1] of physical and mental symptoms occurring in the ten days or so immediately before the menstrual period and usually abating dramatically with the onset of the flow. This syndrome was the subject of an annotation in these columns two years ago,[2] but has otherwise received little attention in Britain. The two papers in this issue of the *Journal* describing this common condition and its treatment are therefore to be welcomed. Dr. Raymond Greene and Dr. Katharina Dalton offer the viewpoints of physician and general practitioner, while Dr. Linford Rees writes as a clinical psychiatrist, but there is close accord between their respective ideas on aetiology, symptomatology, and treatment.

In the premenstrual tension state there may be a preponderance of psychic symptoms such as mental tension, irritability, depression, insomnia, and emotional outbursts, but somatic symptoms, including headache, dizziness, nausea, lower abdominal fullness, oedema, mastalgia, thirst, and easy fatigue, are nearly always present. The time of onset of these symptoms is usually but not always immediately premenstrual, but their recurrence is characteristically cyclical. Menstruation itself is nearly always normal in frequency and duration. The degree of disability varies from patient to patient, but it has been estimated that the symptoms occur in some degree in at least one-third of otherwise healthy women.

The aetiology of the syndrome is still not completely understood, but several contributory factors are apparent. That water retention is an important feature is indicated by the frequency with which gain in weight, oedema, and oliguria mark the onset, and diuresis and loss in weight accompany the decline of each attack. But water retention is not the sole factor or the basic fault, for measures taken to discourage or counter it while relieving the physical rarely affect the mental symptoms. Further, the water retention is associated with changes in sodium metabolism and is accompanied by manifestations of autonomic imbalance, and all of these are influenced by hormonal factors. It is natural therefore to look for some endocrine upset to account for the development of this syndrome and for some method of remedying the hormonal imbalance to relieve it. Drs. Greene and Dalton and Dr. Rees suggest as pathogenetic an abnormally high oestrogen–progesterone ratio, a hypothesis that differs little from Frank's attribution of the symptoms to hyperoestrinism in 1931. That there is an undue preponderance of oestrogen in this condition is supported not only by laboratory data but also by clinical evidence presented in these two papers. For example, primary spasmodic dysmenorrhoea occurs only in ovular cycles in which the oestrogen–progesterone ratio is likely to be normal. Greene and Dalton found dysmenorrhoea in only 2 of their 84 patients and then only in slight degree; and they, as well as Rees, noted that treatment with progesterone, although relieving the presenting symptoms, occasionally brought on dysmenorrhoea.

If these hypotheses are valid, the rational treatment is to restore the oestrogen–progesterone balance. This can be done by supplementing the supply of the latter artificially, and indeed there have been several previous reports of the efficacy of progesterone therapy. Greene and Dalton cured nearly half of their cases and obtained improvement in another one-sixth by giving a daily dose of 50 mg. of ethisterone orally for 12 days beginning on the fourteenth day of the cycle. In severe or resistant cases progesterone had to be injected or, more conveniently, implanted, but altogether in only 3 of their 78 cases followed up were progesterone and ethisterone completely ineffective. Dr. Rees also obtained good results, and with the smaller daily dosage of 5–20 mg. of ethisterone 85% of his cases obtained significant relief. An alternative method of restoring the oestrogen–progesterone ratio to normal is to counter the relatively high level of the former by giving androgens, and Dr. Rees confirmed that methyl testosterone is at least as effective as progesterone. Methyl androstenediol might be preferable to testosterone for this as for other gynaecological disorders, because it is less likely to produce masculinization or to increase libido[3]—the latter a point of importance, for increased sex desire is not uncommon in the premenstrual tension syndrome.

[1] *Arch. Neurol. Psychiat.*, 1931, **26**, 1053.
[2] *British Medical Journal*, 1951, **1**, 1068.
[3] Kupperman, H. S., and Goodman, S. J., *Amer. J. Obstet. Gynec.*, 1953, **65**, 141.

It has been claimed that the emotionally unstable are particularly liable to develop the premenstrual tension state ; that sexual maladjustment, marital disharmony, or continued frustrations are responsible for its onset ; and that psychotherapy must therefore be the first line of treatment. Dr. Rees discounts these claims. He believes that, while psychogenic and personality factors play a part in the syndrome, premenstrual tension is not primarily a neurosis, and that psychotherapy has but a limited, though important, role in its treatment.

The premenstrual tension syndrome therefore is a common condition, although complained of infrequently. And when some of the symptoms are described by the sufferer it is understandable by their nature that they may be discounted by the practitioner as unlikely to have a physical basis. But awareness by both patient and doctor that this is a condition which occurs frequently, which deserves diligent inquiry, which causes much misery, and which responds well to a simple form of treatment could do much to alleviate the suffering not only of the victim herself but also of her household.

EXTRAORDINARY GENERAL MEETING

On Tuesday of this week there was a Special Meeting of the Conference of Representatives of Local Medical Committees in the morning and an Extraordinary General Meeting of the Association in the afternoon to consider the implications of the following resolution put forward by the requisitionists of the latter meeting:

> "That the Association, being concerned by the modification of the present method of remuneration by capitation fees agreed in the Working Party's report, requires the Council forthwith to approach the Minister of Health with proposals for the better protection (financial and otherwise) of the small-list doctor and of the doctor newly seeking entry into practice, and requests the Minister of Health not to implement the Working Party's report until the scheme for distribution of remuneration has been considered in the light of such proposals, and meanwhile to continue the present method of payment."

At the Conference (see this week's *Supplement*, page 206) Dr. Talbot Rogers, chairman of the G.M.S. Committee, gave a calm and reasoned statement of the various negotiations in connexion with the Danckwerts award and its distribution. He pointed out that the implementation of the award depended on a scheme of distribution which would be acceptable to the medical profession, the Minister of Health, and Parliament. It was obvious that any solution could not be expected to satisfy everyone. Fears were expressed that doctors with small lists, or at least some of them, might suffer hardship ; hence the rider of the G.M.S. Committee in relation to this group. The G.M.S. Committee had set up a small subcommittee composed of the medical members of the Working Party and representatives from the Medical Practitioners Union, the Assistants and Young Practitioners Subcommittee, and the Amending Acts Committee to look into the problems affecting the small-list doctor. The subcommittee found the situation much more complicated than it had thought it would be. The small-list doctors did not fall into any one category. The number of those who might suffer could not be exactly ascertained. The amount of money that might be available to those suffering hardship could not be precisely assessed. Dr. Rogers gave some of these and other facts to the Extraordinary General Meeting on Tuesday afternoon (see this week's *Supplement*, page 205). He reminded his audience that in 1951 Mr. Hilary Marquand agreed there was a case for increasing the remuneration of general practitioners, agreed to arbitration, and said that any award would not be paid out unless there was agreement on its distribution by a working party composed of representatives of the profession and of the Ministry of Health. The Working Party was to devise a scheme of distribution which would ease the entry of new doctors into the Service, would discourage the building of large lists, and would encourage group practice and help those least favourably placed. Dr. Rogers told the meeting that he himself had insisted that if the Working Party could not reach agreement on a scheme of distribution the scheme itself should also go to arbitration. He admitted there might have been some hurry in getting the scheme agreed to, but this was necessary in view of the approaching summer recess of Parliament last year and of the urgent desire of the profession for concrete results. Dr. Rogers reiterated what he stated in the morning—namely, that it had been impossible to find a solution of the small-list problem before April 1, 1953, when the new distribution scheme came into operation. Until that date they could not have obtained the necessary information ; for example, it was known only this week that there were a number of new principals in the Service, and this alone would determine the final settlement for the coming year—a fact which would have a bearing on the money that will be available to do justice to those small-list practitioners at present suffering hardship. They had, he continued, recently asked the Ministry of Health to call together the Working Party once more, and this body was already in the process of getting exact

information on which to base action. Any financial readjustments that would be made when the inquiry was completed would be retrospective to April 1 of this year. He saw no difficulty in securing sufficient money to remedy any existing injustices out of the sum set aside for the purpose and also out of the increased money for final settlement.

Under the chairmanship of Dr. E. A. Gregg, the Extraordinary General Meeting was conducted in a calm and orderly fashion, and the pros and cons of the resolution before the meeting were discussed in a spirit free from bitterness. This was due in no small part to the admirable way in which Dr. W. J. Grant, of Shrewsbury, proposed the requisitionists' resolution. He claimed that the method of distribution penalized those with a list of 1,500 or under, and said he was satisfied that some doctors were now underpaid as the result of the Working Party's scheme. He insisted that there should be equal pay for equal work, and that the Government should provide extra inducements to attract doctors into difficult areas. It was wrong, in his view, to try to effect redistribution by economic pressure. He criticized the proposals in the rider of the G.M.S. Committee as a form of charity, and in particular challenged what in effect was a means test to which the small-list doctor should be subjected before financial readjustment could be made. He pointed out that the Danckwerts award had been based on an assessment of general practitioners' remuneration from all sources. Dr. Schiff, who seconded the resolution before the meeting, referred to the agreement in 1949 that in any increased remuneration the loading should be on the first thousand. Dr. Talbot Rogers pointed out that their approach to the distribution scheme had to be based on the terms of reference of the Working Party, and in 1951 both the Conference and the Representative Body gave the medical members of the Working Party full power to use their own discretion in devising the method of distribution.

Lord Horder's amendment, to which reference was made in last week's *Journal*, was accepted by the meeting, as was a similar amendment in reference to the machinery of approach to the Ministry of Health. But by the time the amended resolution was put to the vote it was clear that the great majority of those present were satisfied that the G.M.S. Committee and the Working Party were setting about their task on the right lines to remove any existing injustices. In fact, when Dr. Grant replied towards the end of the meeting he said that he personally did not mind whether or not the meeting passed the resolution, because he and his fellow requisitionists had secured what they wanted—namely, that this problem should be fully debated, and that something should be done about it. The Extraordinary General Meeting did at least succeed in doing one thing, and that was to bring into the open the fact that the Association was as much concerned about the position of minority groups in the profession as it was about the majority. It is to be hoped that before long those adjustments will be made which will put at rest the minds of those, however few of them, who are now suffering financial hardship because of a scheme of distribution that is acceptable to the majority of general practitioners in this country.

POLYMYXIN

The first antibiotic ever shown to exert a systemic antibacterial action—gramicidin—was derived from a *Bacillus*. While combing the microbic world for further antibiotics—a search which began when the powers of penicillin were recognized—this genus was not neglected, and many species or strains have been found to yield substances with a powerful action on various other bacteria, including in some instances tubercle bacilli. That none of these has come into such general use as the better-known antibiotics is due largely to misgivings about their toxicity : all are polypeptides, and the organ which they are generally apt to damage is the kidney. The most promising among them, and now regarded by some workers as having an assured place in therapeutics, are bacitracin and the polymyxins. It is interesting that these two very similar substances, derived from closely related organisms, should have totally different ranges of activity : the organisms most sensitive to bacitracin are Gram-positive cocci, and to the polymyxins Gram-negative bacilli.

The history of the polymyxins is highly confusing, chiefly because there are five of them differing in amino-acid content and in biological effects, both antibacterial and toxic. Earlier studies were made with what is now known as polymyxin A, originally called in Britain aerosporin, and the observed toxic effects of this substance discouraged further progress and delayed the acquisition of our present knowledge. An account of these developments and of the properties of the five polymyxins now recognized has been given by Brownlee and others.[1] Those most suitable for clinical use are B and E, and there is now some clinical evidence of their utility and of their safety under certain conditions of dosage. The specific infection where they are most clearly indicated is that due to *Ps. pyocyanea*, since this organism is highly sensitive to polymyxin and often resistant to all other forms of chemotherapy. Its three main spheres of activity all happen to be amen-

1 *Brit. J. Pharmacol.*, 1952, **7**, 170.
2 *Lancet*, 1951, **2**, 137.
3 *J. Lab. clin. Med.*, 1951, **37**, 402.
4 *Arch. intern. Med.*, 1952, **89**, 90.
5 *Lancet*, 1953, **1**, 110.
6 *Biochem. J.*, 1952, **51**, 558.
7 *Brit. J. exp. Path.*, 1949, **30**, 407.
8 *Brit. J. Pharmacol.*, 1951, **6**, 417.
9 Gowans, J. L., *et al.*, ibid., 1952, **7**, 438.

able to treatment other than by the administration of full doses parenterally. These are, first, superficial infections which can be treated by local application. The value of this procedure in burns has been demonstrated at the Birmingham Accident Hospital by Jackson and his colleagues.[2] Secondly, meningitis can be treated by intrathecal injection. And, thirdly, there are the urinary infections, which call for comparatively small doses intramuscularly. It is hence not surprising that clinical reports such as those of Kagen and others[3] and of Jawetz[4] are chiefly on these forms of treatment, the parenteral dosage (if any) being only moderate and the absence of renal toxicity perhaps no guarantee that larger doses would prove equally safe.

It is therefore of some importance that Swift and Bushby[5] are able to report having treated 53 patients with polymyxin E and 32 with polymyxin B without causing apparent renal damage in any of them. They were mainly children, who were given up to 12,500 units per kg. body weight four-hourly for five days or longer. In one case protein, casts, and red cells appeared in the urine but were apparently attributable to another cause. Other toxic reactions, chiefly pain and induration at the site of injection and fever, were much less often caused by polymyxin E than by B. Nervous effects, such as flushing, itching, and paraesthesiae, were judged to be produced in an equal degree by both, so far as could be ascertained among patients of whom many were too young to describe their sensations.

If these findings are held to prove that polymyxins B and E are not toxic to the kidneys, the conclusion is both important and somewhat unexpected. Hitherto all the polypeptide antibiotics have seemed to suffer from this disadvantage, and fractionation of them has failed to yield a component which retains antibacterial activity and lacks toxicity. Thus, according to Callow and Work,[6] of three licheniformins, A is the least toxic but nevertheless causes renal damage. Marston and Florey[7] report very similar findings with proactinomycin, and Newton and others[8] with bacitracin. Nisin, although it has not been fractionated, is another polypeptide with renal effects which debar its systemic use.[9] If polymyxins B and E are an exception to this rule, they certainly deserve a place in therapeutics, and it is to be hoped that supplies of one of them—preferably, according to these findings, E—may be made available for further study and for general use in those difficult and sometimes desperate cases where no other antibiotic will serve.

TENDON TRANSPLANTATION IN POLIOMYELITIS

Since the original work of Nicoladoni in 1880, opinion on tendon transplantation has passed through the three phases that usually follow the introduction of any new surgical procedure—enthusiastic optimism, disillusion, and now cold revaluation. To study the effects of tendon transplantation in cases of poliomyelitis is particularly difficult, for seldom is it a question of finding a substitute for a single paralysed muscle or group of muscles, but rather of readjusting the balance of an incompletely paralysed limb. The procedure is therefore often accompanied by stabilizing operations on one or more joints. While the fixation of a joint results in an economy of muscular effort, and so may free a muscle for transference, it makes true assessment of the result more complicated. Because surgery is often carried out in childhood and adolescence, the follow-up is long and also made difficult by the migration of patients. The observations of the Poliomyelitis After-Care Programme in Vermont[1] (established by Lovett, co-author with Robert Jones of *Orthopaedic Surgery*, after an epidemic in 1914 and continued by Ober), and those of the Poliomyelitis Clinic in Boston,[2 3] cover not only an unusual length of time but an unusual number of cases which have been systematically treated and observed.

Because the variety of procedures used in treating the upper limb is greater than in the lower, the results of treating the lower limb can be followed up and compared more satisfactorily. Paralysis of the hip and calf inevitably affect the stability of the knee and must be corrected before a transplant round the knee-joint can be undertaken and its results judged. (It might be mentioned that the size of the quadriceps has perhaps led some workers to overrate its importance in the act of walking.) The most commonly used muscles are the tensor fasciae latae and sartorius; the biceps femoris, although an antagonist, is better. It is disappointing to note that even the ability to extend the knee against gravity does not necessarily enable the patient to discard his irons. Objectively the results are disappointing, only 30% of patients regaining active extension, but subjectively the results are good because of the increased feeling of stability at the knee.

The operations performed round the ankle may be grouped together, being designed to restore dorsiflexion, to restore plantar-flexion, or to stabilize the forefoot. The restoration of strong plantar-flexion, the most difficult result to achieve, is desirable, but it is not necessary for a good gait; transplantation of both tibialis posterior and peroneus longus is necessary for success, and in only one case did this enable the patient to balance actively on tip-toe. More helpful to the development of a good gait is the return of dorsiflexion, and it is more easily accomplished by transplantation of the peroneus longus. This, combined with a stabilizing procedure, gave a good result in almost two-thirds of the cases. Tendon transplantations round the forefoot are often combined with a variety of stabilizing procedures and are difficult to analyse. The muscle most commonly transplanted is the tibialis anterior to prevent inversion of the foot.

Surgical technique for transplantation has become standardized. Synergistic muscles are used rather than antagonists, and all transplanted tendons should be anchored to bone. Before the age of 11 the balance of muscle power and bone deformity cannot be accurately

[1] Kuhlmann, R. F., and Bell, J. F., *J. Bone Jt Surg.*, 1952, **34**, 915.
[2] Broderick, T. F., jun., *et al.*, ibid., 1952, **34**, 909.
[3] ——— ibid., 1952, **34**, 900.

estimated, and operative treatment before this will necessarily be uncertain, some 80% of patients requiring further surgery. Stabilization alone will give a good functional result in many cases. Nevertheless, the combination of the two procedures, though suitable only for cases with muscle imbalance, has a valuable place in poliomyelitis aftercare.

TEN YEARS OF "NUFFIELD"

It was in 1943, in the middle of the war, that the Nuffield Foundation was established by Lord Nuffield, and it is now nearing the completion of its second five-year programme. The two programmes have not been greatly different. In the first the emphasis was on normal health, especially child health and industrial health, but also on one specific disease—namely, rheumatism, the work on which was facilitated by a benefaction of £450,000 by Captain Oliver Bird, M.C. Up to the present nearly a quarter of a million pounds have been spent by the Foundation on research into rheumatism, including the financing of a pioneer centre at Manchester and the initiation of a scheme of fellowships. A beginning had been made in fundamental research into causes and in scientifically controlled trials of existing forms of therapy when the work on cortisone and A.C.T.H. was announced from America. Elaborate trials have been made with these hormones, which are described in the recently published review[1] as "certainly not a cure but perhaps a tool." Rational treatment based on a knowledge of causation is not yet possible in rheumatism, and the claims for the many methods of therapy in clinical use are still difficult to assess. Studies are continuing in the hope of throwing light upon the structure of tissues and the processes of rheumatic diseases which involve and damage them.

In its second five-year programme the Foundation has shifted its emphasis to biological and sociological studies. Grants have been made for investigations into cellular biology, microbiology, comparative endocrinology, immunology, and neurophysiology. In these fields, again, the research is recent and the results not yet ready for reporting. Investigations into sociological, economic, and population problems have also been generously assisted. An important object enjoined upon the Foundation by its trust deed concerns the care and comfort of the aged. This review points out, what is often overlooked by those who express alarm at an ageing population, that it is not merely life which is being prolonged but working capacity. Continued and normal activity by the elderly is an important contribution both to their own morale and to the economic well-being of the community. It is from this point of view that the Foundation is proceeding. It is financing research by psychologists at Cambridge into the manner and the rate in which skill declines with age, and into the methods by which the elderly can be helped to continue in work or to change to tasks better designed to take account of any falling off in skill.

Finally, the Foundation has made a major part of its activities the award of fellowships and scholarships both for residents in the United Kingdom and in other parts of the Commonwealth. Over £600,000 has been set aside for these awards from the income of the Foundation during the past ten years, but the aim has been the creation of carefully selected and often short-term and experimental schemes rather than an omnibus endowment. These ten years have been a preparatory period. Readers of the report may wonder what vast achievements for human welfare will be recorded in a review of the Nuffield Foundation to be published at the end of this century.

[1] *The Nuffield Foundation. Ten-Year Review, 1943 53*, 1953, Oxford.

THE MIDDLE-AGED MAN

The inevitable changes attending the contraction of life in its second half come gradually and without fuss in well-adjusted people. But the outlook is very different for the maladjusted, who interpret the normal changes as symptoms of disease. Their lives are darkened by hypochondriacal disturbances and depressing reflections. Illness to many people implies an external agent. The unhappy middle-aged woman blames "the change of life," and is thereby blamelessly exonerated from responsibility. The notion of a male climacteric is in a like category. In the literature (and in advertising circulars) the term male climacteric is becoming familiar. Is there any such condition even remotely similar to the female climacteric?

Claims have been made,[1,2] and denied,[3,4] that there is a rare syndrome properly described as the male climacteric. The symptoms of the presumed syndrome, briefly, are depression, irritability, lack of concentration, palpitation, weakness, and sexual impotence. All of these are present in the neuroses and in involutional depressive states, hence an objective test is recommended—namely, testicular biopsy and the results of testosterone propionate therapy. These, and chiefly the latter, are thought to provide conclusive evidence. These claims, however, have been refuted by other workers unable to corroborate them. The so-called syndrome, they assert, is a psychiatric illness. One advocate for the syndrome asserts that involutional melancholia has "a definite endocrine origin" and advises injections of testosterone propionate.[5] Yet doctors who have to treat involutional melancholia in either sex prefer E.C.T., which gives its best results in this condition. Ageing is a complex but normal process, and it might be assumed that all glands of internal secretion take part in it. The menopause is not a disease entity despite its occasional association with nervous and other complaints. No one has described a condition in men with disturbance of hormone secretion as the only symptom of the so-called male climacteric. Landau[3] and others who regret the use of this inexact terminology believe that the beneficial effects which sometimes accompany injections of testosterone propionate are due to the influence of suggestion on emotionally unstable persons, and that the term should be abandoned.

[1] Heller, C. G., and Myers, G. B., *J. Amer. med. Ass.*, 1944, **126**, 472.
[2] Reiter, T., *Practitioner*, 1953, **170**, 181.
[3] *Med. Clin. N. Amer.*, 1951, **35**, 279.
[4] McCullagh, E. P., *Cleveland Clin. Quart.*, 1946, **13**, 166.
[5] Werner, A. A., *J. Amer med Ass.*, 1946 **132**, 188.
[6] Kinsey, A. C., *et al.*, *Sexual Behaviour in the Human Male*. Philadelphia and London: W. B. Saunders Company. 1948.

Evidence has been obtained[6] that sexual energy falls steadily from the teens to the seventies. The study of spermatozoa counts and excretion of androgenic and gonadotrophic material in urine supports this observation. From this it might be inferred that the changes which some workers assume to be pathological are part of the normal ageing process in which all functions of the mind and body share. Until an occult deficiency of testicular androgen—provided this can be estimated—is shown to bear a direct causal relation to the multiplicity of symptoms embraced by the term male climacteric, we have no ground for accepting the concept.

TEACHING PUBLIC HEALTH

The report on the work of the London School of Hygiene and Tropical Medicine for the year 1951–2 describes once again the activities of this enterprising institution, with its thirteen separate departments and its farm field station near St. Albans. In their introductory remarks Sir Archibald Gray, the chairman of the board of management, and Dr. Andrew Topping, the dean, refer to the effect of increasing costs on the finances of the school, whose credit balance was unfortunately converted into a deficit during the year. Efforts are being made to reduce expenses, but the tutorial fees, which have not been changed since 1930, will have to be increased for some of the courses beginning next October.

The report of the work of the department of public health is of special interest this year, for Professor J. M. Mackintosh has taken the opportunity to review developments during the past twenty-five years. Before the first D.P.H. course was held an informal committee of Professors Greenwood, Topley, Jameson, and Delafield was appointed to consider the future curriculum, and it was in 1931 that the decision was reached that a course of university standard could not be conducted on anything but a whole-time basis. It was about the same time that the General Medical Council published new rules allowing whole-time students to complete the course in nine months instead of one year. As the years went by the tendency was always to reduce the number of formal lectures and to make the course more tutorial in character. At the present time the greater part of the teaching is based on the study group system, which allows students to choose the subjects to which they would like to give particular attention. At the end of the 1939–45 war the whole curriculum was revised. Demonstrations of bacteriological techniques and of the chemical analysis of water and milk have taken the place of the intensive exercises in practical work which were such a time-consuming part of the diploma courses before the war, and the first term is now occupied with "a general introduction to the scope and character of the public health and social services." During the other two terms the student is brought closely into touch with the practical problems of public health administration by working under the supervision of medical officers of health. In addition, study groups are formed and the students themselves plan and execute investigations into some problem allied to public health. An "overwhelming" majority of students found that learning through study groups was more interesting than traditional classroom work and 55% thought it to be more effective. The range of studies is gradually being extended, and in the current course the medical aspects of airport control and a discussion of general practice were introduced for the first time. "These various additions to the programme," the report states, "would overburden the course if rigidly enforced on all the students, but they are presented in the spirit of elective studies and are accepted as such by the students whose maturity and experience enables them to be selective in their interests."

These new methods of teaching public health and the swing of emphasis from some subjects to others reflect the present changing views about social and preventive medicine. The London School of Hygiene and Tropical Medicine has always been ready to move with and even ahead of the times. The present report shows that this policy has been fruitful and will continue.

COST OF PRESCRIBING

In the first full year of the Health Service general practitioners' prescriptions cost £35m. It is estimated that in the current year the cost will be about £52m. When the sum of £6.7m. (estimated) is taken off for patients' payments, the net cost to the taxpayer is still £10m. more than in 1949–50. Analysis shows that three-fifths of this total is accounted for by the cost of ingredients and not by chemists' fees.

In the summarized accounts[1] of the National Health Service for 1951–2 the Comptroller and Auditor-General states that in the thirteen months up to December 31, 1952, 282 general practitioners were reported for apparent excessive prescribing. All but eleven of these reduced their prescribing costs after warning from the Ministry and—to quote the Comptroller and Auditor-General—"without detriment to the treatment of the patients." That only a minute proportion of general practitioners were thought to be prescribing excessively gives the lie to any accusations that the size of the nation's drug bill is caused by general extravagance among doctors. Note must be taken, too, of the statement that the reduction in the prescription costs after warning of certain doctors was achieved without detriment to their standards of treatment. This may be true, but we must never depart from the recognition of the right of the doctor to be the sole arbiter of what is best for his patient. To surrender this fundamental principle would cost far more than the few thousands saved on cheaper prescriptions. Yet responsibility for one-eighth of the expenditure on the Health Service is in the hands of general practitioners, though there are reasons for this high cost which do not reflect on the prescriber, and there is no single way to economy, but most general practitioners know that there are many small ways and means of saving. Those who do not know should make it their business to find out. "Many a mickle makes a muckle."

[1] Published by H.M.S.O., London.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

HYSTERIA

BY

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Hysteria has been known since antiquity. Its symptoms, often dramatic and apropos to the times, have compelled attention and wonder. It has had many explanations. For our present views we owe a debt to both neurologists and psychiatrists, amongst whom in the past hundred years the contributions of Charcot, Janet, and Freud have been outstanding. Treatments, lay and medical, have been as various as the theories about its aetiology. Physicians and ministers of the traditional religions have relieved many sufferers from hysteria, as also have less orthodox faiths and modes of healing. That many of these treatments have not proceeded along rational lines and have produced symptomatic improvement without insight does not by any means wholly detract from their practical usefulness.

Hysteria may appear in the form of physical or psychological disorder. The patient's emotional disturbance, which is fundamental to the illness, may be more or less completely converted into physical signs or symptoms (conversion hysteria) or it may find more direct expression in episodic mental states of a characteristic type. Overt anxiety or even panic may accompany hysterical symptoms.

The Hysterical Personality

Frequently, though by no means invariably, those who develop hysteria have shown before the onset of the illness an aggregation of traits which has been called the "hysterical or histrionic personality." It is often evident that these people, usually women, though adult in age, are to a great extent dependent still on one or other parent. Their temperaments are quicksilver, over-sensitive, over-responsive. They often fall into passionate attachments, as intense as they are transient; they make excessive demands on others, and, disappointed in their unrealistic expectations, react impulsively in spite and pique; and they attempt continually to dominate others by their whims and moods. Abnormally self-centred and vain, they seem to feel an almost constant compulsion to bolster up their egos by holding the stage and playing out dramatic roles evolved by their too vivid hopes and imaginations. Their capricious and frequent lying has often the fantastic and innocent quality of the child's. Sexually they are superficially excitable but fundamentally inhibited. Behind all this, hidden from the patient's unassisted insight, there seems to be an intense longing and need for attention and love—a need infantile in its exclusiveness and which is as great as their ability to feel deeply towards others is small. It is not surprising, then, that the environment they inhabit is more often than not emotionally on the boil. These people easily provoke antagonisms, are very difficult to live with, and difficult to be patient towards in treatment. It is salutary, therefore, always to consider such a previous personality as an essential part of the illness.

The particular symptom developed depends on one or more of several factors: it has often clearly a symbolic meaning (for example, hysterical blindness may symbolize an inability to contemplate some unpleasant reality); it may be an exaggeration of some physiological reflex (for example, hysterical vomiting) or may utilize some locus of earlier disease or injury; or it may be the outcome of suggestions derived from the illness of a near relative or friend, or from previous medical examinations. It is advisable always to ask the patient what he thinks is wrong, and to find out if anyone in the patient's environment has suffered from anything similar. All neurotically ill people are suggestible, and, identifying themselves emotionally with others, may imitate their disabilities. The greater the individual's knowledge of special kinds of disease, the nearer his symptoms will mimic those diseases. Gross hysterical symptoms seem now to be less common than formerly, when they were often produced by unskilled and over-enthusiastic examination.

Physical Symptoms

Physical symptoms are usually in the nature of some incapacity, partial or complete, involving the sense organs or voluntary musculature—aphonia, mutism, deafness, blindness, paresis, or anaesthesia. The disability is often of sudden onset, its degree and extent tend to be variable, and its details do not coincide with the signs of neurological disease. For example, the hysterically mute individual can cough normally and may be persuaded to write his replies to questions; the sufferer from hysterical blindness may avoid obstacles in his way; the muscles of a hysterically disabled limb may be used in some movements and not in others; the anaesthesia corresponds in its distribution and in the types of sensation involved to no recognized variety of organic sensory loss.

In other cases movements may, instead of being diminished, be increased in the form of tremors. Hysterical disturbances of gait may be bizarre; other abnormalities of movement or posture—for example, tics and dystonias—may also be hysterical but are more often symptoms of organic involvement of the nervous system. Sensation also may be heightened or perverted, localized areas of hyperaesthesia may be described, and head pains or abdominal sensations complained of. In these cases the paraesthesiae are frequently reported by the patient in hyperbole: they are constant, may even be claimed to be present during sleep, and are intolerable; analgesics have little or no effect on them. All these symptoms become aggravated under observation and fixed by too often repeated examination.

The visceral symptoms of hysteria most often encountered are persistent vomiting and anorexia. Hysterical vomiting, often unaccompanied by nausea, occurs after meals and is effortless. Anorexia nervosa commonly manifests itself in a striking combination of emaciation and continued, even apparently tireless, activity. Found typically in girls and young unmarried women, this condition is not so difficult to distinguish from Simmonds's disease as is often supposed.

Mental Symptoms

The commonest mental symptoms are amnesias, fits, and disturbances of consciousness—fugues, stupors, and so-called twilight states.

Hysterical amnesias may be localized, covering some particular event, or (rarely) very extensive, involving even the whole of the patient's past life and so resulting in loss of identity. A localized amnesia may cover an incident involving guilt, and sometimes a criminal act—for example, amnesia may be claimed for the circumstances of a culpable accident, the patient saying that he suffered a "black-out." The assessment of such a black-out will centre on the

investigation of the possibility of concussion and on the history of previous similar attacks. An amnesia involving the whole of the past life of a young person is invariably hysterical.

Hysterical fits are diurnal. There is usually no typical clonic–tonic succession as in the epileptic fit, and self-injury is unusual. Tongue-biting, incontinence, and transient reflex changes do not occur. The seizures are seldom followed by complaints of headache and confusion. There is always an audience, and if attempts are made to restrain the patient he responds with wild struggling. Atypical faints and vaguely described collapses also occur commonly.

Hysterical disturbances of consciousness of longer duration may be associated with immobility, with dramatic posturings and verbal outpourings, or with wandering (a fugue). These always require expert assessment.

There is in all hysterical reactions a great tendency towards exaggeration, and the patient in his bids for attention may go so far as self-injury. Cases of dermatitis artefacta and other types of minor wounding are allied to the hysterical reactions. Suicidal gestures or attempts may also be made by individuals of hysterical personality when some thwarting produces great excitement. These attempts are usually impulsive : though they may not always be very serious, they are danger signals and urgent calls for help, and should not be dismissed as innocuous.

In sufferers from hysteria the typical mental attitude, *la belle indifférence*, is not always found. In the early stages there is often a good deal of anxiety. It is only when the establishment of symptoms has provided the terms of a truce for the conflicting emotions that a surface calm is achieved and the patient presents an attitude of bland acceptance of his disabilities. The lack of insight is then typical. The hysteric describes at length a number of painful or discommoding symptoms and goes on to state that he is not worried by them : he does not consider his symptoms nervous, declares in a sweeping way that he has had no recent anxieties, and seeks purely physical explanations for his sickness.

Diagnosis

Hysterical symptoms, which are commoner in women than in men, are developed most often around puberty and adolescence and in early adult life. They are uncommon after middle age. When occurring for the first time after the age of 45 they should be regarded as organically determined, unless the opposite has been clearly proved.

A careful physical examination is essential in every case. Hysteria is often mistaken for physical disease, and physical disease is often called hysteria. It would be profitless to attempt a list of the syndromes which may cause confusion. In perhaps the most difficult cases the question of organic neurological disease is at issue: disseminated sclerosis, brain tumour, encephalitis, myelitis, cerebral vascular disease, myasthenia gravis, and many other physical processes may be misdiagnosed. The situation is also complicated by the fact that organic brain disease may itself cause or release hysterical symptoms, and hysterical symptoms may be grafted on to the physical effects of an injury. It is helpful to remember that in a young person organic neurological disease does not usually develop so rapidly as hysteria ; that there are no significant reflex changes in hysteria ; and that the physically ill individual usually shows some general evidence of physical illness. It is surprising how often the eliciting of a story of some recent emotionally disturbing event leads to the forgetting of the platitude that a physical illness has also to begin some time.

Hysteria must be distinguished from other kinds of nervous and mental illness, but too precise a pigeon-holing of neurotic reactions is impossible, since many of them show an admixture of anxiety, hysterical, and obsessional symptoms. It should, however, be determined whether or not the hysterical symptoms are primary and predominant: appropriate treatment depends on this. Hysteria mimicking severe mental illness is much less common than is widely believed. Fugues should not be lightly discounted as hysterical: many have a depressive basis and are suicidal equivalents.

The differential diagnosis between hysteria and epilepsy is often difficult. Some of the distinguishing features have been described already. An electro-encephalogram may be helpful, and an accurate description of the attacks by a witness always is.

Close attention to the patient's symptoms and appreciation of the setting of his illness are both equally important. Knowledge of the patient's previous personality and a history of neurotic illness help always in assessing present symptoms. But the diagnosis can never be considered to be on a firm basis until the precise emotionally charged situation or dilemma which has precipitated the patient's symptoms has been identified and his symptoms are seen to be understandably linked to it.

Treatment

The general practitioner, acquainted with the details of the family background and the home circumstances, is strategically in the best position to treat hysterical reactions. Unfortunately, inadequate undergraduate instruction in psychological medicine has caused many doctors to feel that they lack the necessary knowledge. Much depends too on the personality of the practitioner, his insight, the direction of his interests and his sympathies, and the pressure of his work. It is better to refer these patients for specialist opinion too soon than too late ; hysterical symptoms, if disabling, should not be allowed to persist. It is pathetic to see women referred for psychiatric treatment after twenty years' history of vague abdominal pains and after "everything's been taken away" by well-intentioned but ill-judged surgery.

The doctor's attitude to this group of people, with their many complaints and clamant demands on his attention, is particularly important. He should be neither censorious nor too kind: if he is the former he will scare people away who genuinely need his help, and if he is the latter he will foster an undue emotional dependence and attachment which may become intolerable to himself. He must be a good listener.

When a current cause of the patient's anxiety can be found his problems must be clearly identified for him, and he should be helped and encouraged to tackle these in a constructive way. This sort of practical guidance, which may have to be repeated often, and the emotional maturation which time may help to bring about lead in a fair number of cases to a satisfactory result. A deeper exploration of the personality and earlier conflicts and traumata, by means of psycho-analysis, may, however, be necessary in some cases. To benefit from psycho-analysis the patient must be young, of at least average intelligence, and willing to co-operate in a long and intensive course of treatment. These requirements limit psycho-analysis to a minority of hysterical patients.

It may be sufficient for cure (particularly in the case of children) to alter the aspect of the environment which has caused the stress: a change of school, removal from danger, more suitable occupation, or the acquisition of a house of one's own may abolish the conflict which was causing symptoms. It is also quite essential for the doctor to promote an understanding attitude in the relatives, and to gain their confidence and co-operation. There is a great tendency for hysterics to adopt in a striking form the social role of the sick person. They are often adept in mobilizing sympathy and notice. They reiterate their desire to get well and back to duty, and are very apt to shift subtly the blame for their lack of progress to aspects of the environment, including the doctor and his treatment. Relatives are thus drawn into the orbit of the illness, come to see the situation entirely through the eyes of the patient, and swaddle him in too much solicitude.

Compensation cases have usually to be referred for a consultant's opinion. Too much hope is often placed in the settlement of a claim; it is in probably the minority of cases that settlement leads to rapid cure.

A thorough physical examination followed by a pronouncement that recovery is imminent may occasionally lead to the prompt disappearance of hysterical symptoms in subjects of low intelligence. But in most neurotic illnesses what is usually called "reassurance" is not enough. The jovial encouragement that there is nothing wrong and nothing to worry about merely convinces the patient that what is wrong has been missed.

Treatment may have quick and even spectacular results, but it may also have to be prolonged, and too great an insistence should not be laid on cures. In most cases, if symptoms are relieved and the patient is helped to function again reasonably happily and efficiently, that should be considered satisfactory. Sedation has a useful part to play in supportive treatment, particularly where there is much anxiety. A mixture containing potassium bromide, 10 gr. (0.65 g.), and chloral hydrate, 5 gr. (0.32 g.), or amylobarbitone sodium, 1 gr. (65 mg.), given three times a day is often sufficient for substantial relief of tension, while in the management of reactions of acute excitement and panic a large dose of a quickly acting barbiturate—for example, pentobarbitone sodium, 3 gr. (0.2 g.), will provide sleep.

It is a mistake to pay too much attention to specific symptoms. Treatment on a purely symptomatic level leads usually merely to the banishment of one presenting symptom and its replacement by another. The disabling nature of a symptom—for example, mutism, deafness—may, however, necessitate a frontal attack on it. In such a case the attempt should be made to eliminate that symptom at a single session. Up to two hours should be set aside, and the doctor's confidence in his success is more important than the method he employs. Firm persuasion and suggestion are usually enough. They may be facilitated by the intravenous injection of a barbiturate (amylobarbitone sodium or thiopentone). It is doubtful if hypnosis is ever essential; it is never the treatment of choice. A localized amnesia may be resolved under barbiturate narcosis, but probably only if the patient is willing that it should be. Losses of identity clear up spontaneously. In some cases the dramatic intervention of the narcosis is a face-saving situation enabling the patient to relinquish a symptom which is no longer useful to him, and it is not necessarily undesirable to allow him this relief.

If further breakdowns are to be guarded against it is important that the patient should gain insight. But many hysterics reject attempts to give them insight, and recoveries occur without it. Insight should therefore be fostered but not too doggedly insisted upon.

Admission to a mental hospital is never advisable, and admission to a neurosis clinic should be arranged only in certain situations and with definite ends in view. It is often necessary where there is loss of identity, a fugue, gross paralysis, or blindness, and always in cases of anorexia nervosa. Admission may also be necessary when the home environment militates against recovery, but it is essential here to estimate whether after the period in hospital this environment is going to be improved or the patient's resources for dealing with it increased. If these precautions are not taken, when the time comes for the patient's discharge he is apt to jib and to become worse, suicidal threats may be made, recriminations are frequent, and the patient finally returns home disappointed, bitterly critical, and more difficult to handle. Admission to hospital is especially profitable where symptoms have developed on a basis of physical debility and fatigue.

Electric convulsion therapy or other "shock" treatment is not helpful.

The doctor may be asked to advise on marriage and child-bearing. Marriage as a medical prescription might well be placed on the D.D.A.: it should not always be discouraged, but it is rarely wise to recommend it. Child-bearing should always await the attainment of emotional stability, which it does nothing to promote.

Prognosis

Prognosis depends not on the particular symptoms but on the stuff the patient is made of and the kind of difficulties he has to surmount. If the environmental difficulties are transient or modifiable the symptoms may be expected to clear up. If the trouble lies not so much in the toughness of the demands of the environment as in the inadequacy of the patient's response the outlook is less favourable. With much patience some of these handicapped people may be guided to be more healthy minded and sensible in their dealings with life's problems. Many have numerous relapses and need much propping. The longer hysterical symptoms have lasted the worse is the outlook: there is a great tendency to chronic invalidism, and the mental reaction may become as malignant as a widely disseminated bodily cancer.

Next Refresher Course Article.—"Carcinoma of the Breast," by Mr. H. J. B. Atkins.

EMPIRE RHEUMATISM COUNCIL

LORD HORDER RETIRES

The annual meeting of the Empire Rheumatism Council was held on April 29 in London. At the meeting Lord Horder, who has been chairman of the council since its inception in 1936, announced his resignation. A message from the Duke of Gloucester, the President, expressed his appreciation of the great leadership and wise guidance which Lord Horder had given over many years. Lord Webb-Johnson said that Lord Horder's decision was a matter of regret to them all, but apparently it was irrevocable. To succeed him he proposed Dr. W. S. C. Copeman, who had been for eighteen years honorary medical secretary of the council and had made valuable contributions to rheumatology. Professor R. E. Tunbridge seconded the proposal, which was carried unanimously. Dr. Copeman, in accepting the office, asked for an assurance—which was given—that the council could continue to look to Lord Horder for assistance and counsel.

On the proposition of Sir Henry Cohen, Lord Webb-Johnson was re-elected vice-chairman, and Dr. Oswald Savage and Dr. R. M. Mason were elected honorary medical secretary and deputy respectively. Sir Adolphe Abrahams moved a resolution placing on record the council's great appreciation of Lord Horder's long and distinguished services. He described him as the "W. G. Grace of Medicine"—one who would never be surpassed. Sir George Elliston also spoke to the resolution.

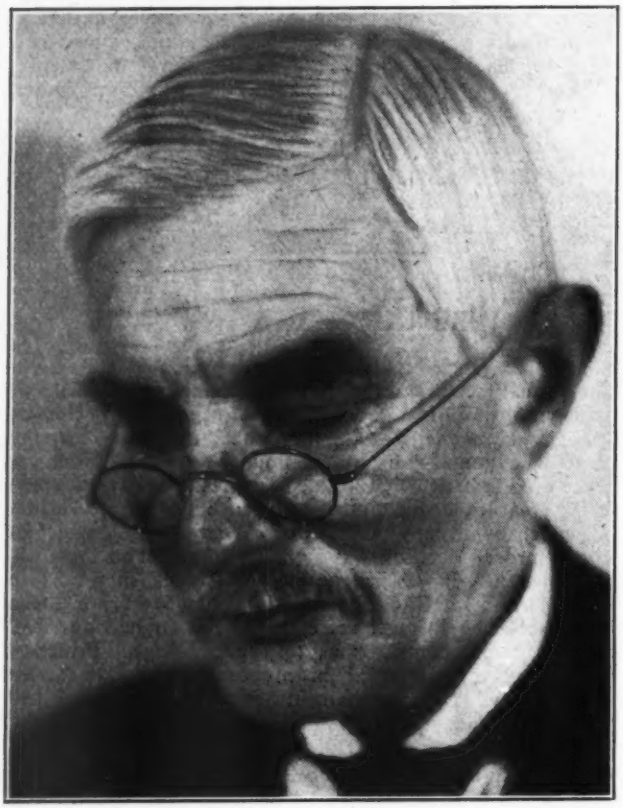
In presenting the financial statement of the council, Mr. W. R. C. Halpin said that there had been an increase during the year of nearly £4,000 received in donations. Donations must form the backbone of their revenue. He was ambitious for an income of £50,000 a year, short of which the council could not open its wings to the full extent. Income last year had amounted to nearly £17,000.

The annual report, which was adopted by the meeting, referred to a generous offer by Merck (North America) Inc. to supply free of charge a quantity of "cortone acetate" tablets sufficient to undertake trials which would keep 50 patients on continuous oral therapy for a year, and after that time to continue to treat *in perpetuo* those of the 50 who still remained on the therapy. Trials were being undertaken to discover the clinical and functional difference between a cortisone-treated group and an aspirin-treated group of patients, and the scheme was coming into operation in nine centres in England and Scotland.

DR. F. PARKES WEBER, 90

On May 8 Dr. Frederick Parkes Weber celebrated his ninetieth birthday. It is just upon 60 years since he became physician to the German Hospital in London. By the later 'nineties he was an ardent participant in the discussions in half a dozen or more medical societies. What has distinguished him during all these years has been his zeal for clinical studies, his search for the more enigmatical signs and symptoms of disease, and the clarity with which he has expounded what he has discovered.

Ten years ago, on his eightieth birthday, his friends at the German Hospital presented him with a volume of his *Collected Writings*—it could be the titles only, for the separate writings ran to nearly a thousand, beginning in



1890 with a contribution to *St. Bartholomew's Hospital Reports* (he was then house-surgeon at St. Bartholomew's) on abnormal foramina in the heart and its valves, and ending in 1943 with a short paper in the *British Medical Journal* on congenital jaundice in a man aged 77. Since then, of course, there have been many further contributions in this and other journals, for Dr. Parkes Weber, who, when he was only 40 or so, wrote for Allbutt and Rolleston's *System of Medicine* all there was to say about the physiology and pathology of old age, has always been at heart a youth, and we can confidently hope that the weight of years will not stay his mental activity. Until a year or two ago he was present at almost every meeting of the Section of Dermatology of the Royal Society of Medicine, and it was always refreshing, and in sharp contrast to the mumbling undertone in which the discussions are often conducted, to hear his resonant speech, with no possibility of mistaking a word, as he compared the unusual case then being demonstrated with one which he had seen anything up to 60 years before. Increasing physical disability has in no way impaired his intellectual energy, the vigour and precision of his language, and his enthusiastic interest, especially in the rarer signs of disease. He is an example of the old-time scholar-physician, pedantic perhaps in the use of words—but then, words to him are real things. A rose by any other name may smell as sweet, but a disease wrongly named may mean a distorted clinical picture. Standing on his feet (later, alas, leaning on a crutch), he would sometimes seem to be coining words and phrases to differentiate and clarify the diagnosis. His paper on naevi, published in the *British Medical Journal* 18 months ago, showed that he was still giving the same careful thought as ever to the classification of pathological conditions.

Dr. Parkes Weber—elected a Fellow of the Royal College of Physicians in 1890—belongs to a generation of medicine which has largely passed away, but the younger generations who have profited from his writings and from the unselfish help he has always given to colleagues and students will acclaim him as a great doctor, a wise philosopher, and a most courteous gentleman. He comes of a long-lived family—his father, Sir Hermann Weber, lived to 95—and his friends will hope that more and happy years remain to him. As he himself put it when he was 80, in speaking of his life as a strenuous holiday like an Alpine walking-tour, "This holiday is not yet over."

HEALTH CONGRESS AT HASTINGS

NEW APPROACHES TO PREVENTIVE MEDICINE

The annual Health Congress of the Royal Sanitary Institute, which was held at Hastings from April 28 to May 1, covered as usual a wide field of preventive medicine and public health services, personal and communal. The subjects discussed in eight sections and four special conferences ranged from building by-laws and modern plumbing to the place of the health visitor in the welfare State, from the control of tuberculosis in Tanganyika to the Middlesex development plan, from a scheme for the part-time employment of ageing persons in Finsbury to the ultra-violet deodorization of the air.

A Disease-proof Nation

The president of the Congress, Lord EUSTACE PERCY, in his inaugural address, posed the question whether the modern human being, artificially immunized against virus diseases, but at the same time carefully protected in childhood against any natural immunization, would prove to be an entirely satisfactory citizen in the future City of Health. The victorious army against the bacillus and the parasite seemed to be exposed to serious flank attacks by other enemies of the constitution whose strength had not been measured—by crippling infiltrations like arthritis, and deadly shock troops like cancer and disorders of the circulatory system. A great Englishman of the last generation had once said to him that he "had never been well enough to be really ill." Was it possible that we were preparing a race of citizens who would never be ill enough to be really well?

"For a disease-proof nation may be a hectic nation, working shorter hours at a more intense and continuous expenditure of energy, mental as well as physical; with a longer expectation of life, but possibly an actually shorter expectation of fitness for work at the new level of intensity; with larger but less reposeful leisure; protected against specific occupational hazards, but more and more exposed to the general hazard of working strain; prone to thrombosis and to nervous or mental breakdown, and making increasing demands on our newly christened science of geriatry. Such a result, to put it mildly, would not be an 'elegant' solution of our national health problem."

A General Practice Teaching Unit

In the Section of Preventive Medicine, presided over by Mr. FRED MESSER, M.P., chairman of the Central Health Services Council, Dr. RICHARD SCOTT described the work of the Edinburgh University general practice teaching unit. By taking a few selected students into association with family doctor practice it had again been demonstrated that medicine was indivisible. "To the doctor examining the patient in the consulting-room or in his house, curative medicine, preventive medicine, and social medicine are academic concepts. What he practises is medicine."

The original general practice unit at Edinburgh consisted of a practice comprising some 2,000 patients and staffed by two doctors, a public health nurse, a medico-social worker (almoner), and a secretary, all of whom were university employees. In addition, the services of a dentist, pharmacist, and chiropodist were available. The team afforded instruction to a limited number of voluntary students. As this instruction was to become a required part of university teaching, and in order that more students might be accepted, a second team, with identical staff and facilities, had recently been added, thanks largely to financial support from the Rockefeller Foundation. Some 15 students were accepted by this unit each academic term. They attended a weekly seminar as a group, and each student was also allotted one session a week, when he was the only other person present while the doctor saw patients who attended without appointment. The method of teaching was to manœuvre the student into a position of clinical responsibility for an individual or a family, and the approach was that of the apprenticeship technique.

In the same section Dr. J. F. WARIN, M.O.H., Oxford, discussing the future of public health services, described himself as "one of the lucky ones," in that while many medical officers of health had lost touch with fever hospitals during the last five years he had been allowed to accept the post of part-time consultant to the United Oxford Hospitals, with clinical responsibility for 36 infectious diseases beds. He was sure that it was just as important as ever for the potential recruit to the public health service to have a good grounding in infectious diseases. A critical review of infectious diseases routine which he had carried out during the last six years in one large and one medium-sized county borough had revealed some "very dusty corners," and he had been amazed at some "prehistoric practices" still in existence. He gave examples of routine procedures of long standing which had served their purpose and might well be discontinued with benefit for all concerned—for example, prophylactic eyedrops for all newborn babies, fumigation of library books, and the like.

Maternity and Child Welfare Services

The integrated service of domiciliary midwifery which was started in Oxford last June, when the health department and the general practitioner went into full partnership, was also described by Dr. Warin. Under this scheme every new patient attending a local authority antenatal clinic is immediately referred to her own doctor for booking in the maternity medical service. She continues to attend the municipal clinic for antenatal care, and then is again referred to her doctor with a detailed report at the 36th week. Most cases are delivered by the midwife, but if necessary the doctor with whom the patient is booked is called in. Post-natal examination is the responsibility of the general practitioner, but the municipal service and health visitors play an important part in encouraging the patient to attend. The scheme was working, said Dr. Warin, to everybody's satisfaction.

In opening a discussion on the future of the maternity and child welfare services, Dr. F. J. W. MILLER, of Durham University, repudiated the idea put forward by some recent speakers and writers that the day of the child welfare service is over, but he felt that a time had come for a frank examination of its problems. He pointed to disappointing figures at child welfare centres in Newcastle; only 30% of the infants were taken to the centre 10 or more times in the year. In health visiting, again, the other pillar of the child welfare service, he found room for improvement; in particular the health visitor should be taken into the confidence of the medical officer of health. Regular visiting in all areas should be replaced by selective visiting, with concentration on the people who did not attend clinics, and in each district, without formal plans being made, the health visitor should be encouraged to get in touch with the family doctors.

The Hospital Paediatrician

A more cheerful picture of infant welfare clinics was given by Dr. MAURICE R. WOODS, who found that mothers of all social spheres attended them. Dr. DOROTHY EGAN, principal medical officer for maternity and child welfare, L.C.C., objected to the proposed taking over of child welfare work by the paediatric staffs of hospitals. Experience had shown that even in the atmosphere of a child welfare centre the hospital paediatrician did not find it easy to adapt himself to a purely educational and advisory role, and the change of emphasis to preventive from curative work would be even harder to bring about within the hospital itself. The general practitioner, she said, should ideally combine curative and preventive work, but if he was to do this health centres must be established and group practice become a reality, and he must be prepared to consult and work with the medical officer of health as a specialist in social medicine and epidemiology. Dr. MARY HELLIER, a general practitioner, said that for some time now a group of medical women like herself had been feeling that there was an urgent need for someone like a social worker to be available to the general practitioner.

From the chair of the section Dr. BERNARD SCHLESINGER referred to "quite unjust recent attacks in the medical press" on infant welfare clinics. At the same time he urged close liaison between the medical officer of the clinics and of the hospitals of the district, and the family doctor should not be left out of the picture. If only the family doctor had the time and also the special knowledge and interest, it would be an admirable thing if he would take weekly sessions at such clinics.

In some further discussion on health visiting Dr. JOHN BOWLBY, of the Tavistock Clinic, urged that health visitors should give more attention to mental health, cultivating especially an understanding of the unconscious processes which affected maternal attitudes. The future role of the health visitor in the welfare State was also discussed. One speaker declared the most serious problem affecting the health and welfare service to be not physical but psychosocial breakdowns. The training of the health visitor in the future should be along lines similar to those of the almoner rather than those of the nurse.

The Medical Officer of Health

From the chair of the Conference of Medical Officers of Health Dr. ANDREW TOPPING, as usual, expressed himself vigorously. The contention that the days of public health were over, he said, was completely untenable. He gave an impressive list of community health problems still to be tackled:

(1) Development programmes for the care and control of mental ill-health.
(2) Environmental conditions at work and in the home.
(3) Epidemiology of non-infectious diseases.
(4) Atmospheric, river, and sea-coast pollution.
(5) Continuous and increasing health education.
(6) Co-education and streamlining of the many diverse health agencies.
(7) The ever growing need for geriatric services.
(8) The correlation and proper recording of the medical findings of infant welfare clinics, the school medical service, the industrial medical service, and the National Health Service, and the linking up of the work of executive councils, hospitals, and local health authorities.

Dr. Topping had also a word to say about the family doctor:

"We all unite in saying publicly that the family doctor is the keystone of the medical arch, and that he is in the forefront of the battle, and nullify our statements by encouraging the public to bow down and worship the Golden Calf of Harley Street. If a man has the urge and the desire to become, say, an anaesthetist, good luck to him! . . . Why, however, should he be looked upon as a being of superior clay to the family doctor, who, we so consistently agree, is the man of greatest importance in the health service, and who must, if he is the right type, combine good medical knowledge with superhuman industry and know-

ledge of applied psychology? The statement 'He's only a G.P.' is heard far too often, and unless something is done to get things into their proper perspective, the general standard of medical care will be seriously prejudiced."

Expertise in one facet of an almost limitless subject should not connote superiority. But Dr. Topping went on to ask why either the consultant or the family doctor should be considered superior to the doctor who elected to specialize in community health—a field almost as wide as that of general practice. The reason was not far to seek—there was nothing spectacular in removing the conditions which predisposed to tuberculosis, but a successful thoracoplasty or an avoidable tuberculous meningitis cured by streptomycin may qualify for a banner headline.

Occupational Health and Housing

Questions of occupational health took a larger place than usual in the Congress. Dr. ANDREW MEIKLEJOHN, president of the section, suggested that too much emphasis was placed on the contribution of medical service to industrial production. Such a contribution would, of course, come about as a result of efficient medical service, but it was not the primary purpose. He also said that the occurrence of accident or disease in industry was too apt to be ascribed to the human element, often meaning by that term a factor beyond control. In fact, not infrequently the cause was just carelessness, indifference to the welfare of others, or plain laziness. In other instances, important to the industrial medical officer, it arose from physical, mental, and social strains, not necessarily a part of the job, but influencing its working efficiency. Dr. Meiklejohn was a little disturbed by the tenor of some of the advocacy for a comprehensive occupational health service not restricted to factories, but embracing all workers, wherever and however employed. The attainment of an occupational health service need not involve emotion or over-statement. It would come about from the workers themselves, who, enjoying the benefits of proper homes which they alone could provide by more urgent effort, would not tolerate inferior or noxious conditions at work.

Several papers dealt with housing, one of them by the Chief Medical Officer of the Netherlands, Dr. C. BANNING, who said that statistics in Holland had failed to reveal a correlation between tuberculosis and bad housing. On the other hand, it had been shown that the children who came to child guidance clinics were in the main children from overcrowded and shared houses. Bad housing conditions played an important part in the field of mental health, and 30% of Dutch families shared their homes with others. A similar theme was developed by Dr. J. V. WALKER, M.O.H., Darlington, who, discussing housing priorities, said that less damage was done (and less housing priority therefore required) in homes with a distressing case of illness, provided there was family affection, than in the household where everybody was at odds, although superficially all appeared to be in reasonable organic health. Psychological strain, he considered, might be a reason for housing priority.

The Ageing Population

A session was devoted to the problem of the ageing. Dr. BLYTHE BROOKE, M.O.H., Finsbury, reminded the Congress that the number of persons over 65 has increased sixfold during the last hundred years; they now account for 11% of the population, and by 1977 may be expected to account for 16%. The proportion is now higher in Great Britain than in any other country except Belgium, though Switzerland comes close. He also pointed out that what these people stand in need of is more than occupation, it is a share in the life of the community.

Medical officers and executives of industrial organizations described various schemes for employing elderly workers.

The final meeting of the Congress was concerned with tropical hygiene, when Dr. JOHN LOGAN, of the Division of Medicine and Public Health of the Rockefeller Foundation, discussed environmental control in the Tropics, its problems and opportunities, and Dr. L. D. KHATRI, deputy inspector-general of the Medical and Health Services of the Hyderabad Government, gave a remarkable account of anti-plague measures in Hyderabad State. D.D.T. was introduced as an anti-plague measure towards the end of 1949, first in Hyderabad city, and then in the endemic zone in the State. In that year the number of plague cases had been 6,858, and the number of deaths 2,069. In 1951 the numbers were respectively 464 and 104, and in 1952 they were 17 and 2. It should be stated, however, that 1949 was a year of political disturbance, and the existing anti-plague organization broke down. The figures for some of the previous years were rather lower, but since 1944 the number of cases had always run into four figures, and only in one year was the number of deaths below 1,000. From September to November, 1952, with timely and intensive treatment with D.D.T., not a single case of human plague was reported.

Reports of Societies

ANNUAL CONGRESS OF THE OPHTHALMOLOGICAL SOCIETY

The Annual Congress of the Ophthalmological Society of the United Kingdom was held from April 23 to 25 at the Royal Society of Medicine. On the first day Dr. A. MACRAE delivered his presidential address on "Prognosis in Malignant Melanoma of the Choroid and Ciliary Body." There then followed a number of short papers. After tea Professor Sir Geoffrey Jefferson delivered the Bowman Lecture on "The Syndromes of the Cavernous Sinus." The annual dinner was held at the Trocadero Restaurant in the evening.

Antibiotics in Ophthalmology

The remaining days were devoted to further short papers, some films and demonstrations, and a discussion on "The Scope of Antibiotics and Chemotherapeutic Agents in Ophthalmology."

Professor ROBERT CRUICKSHANK, who opened the discussion, declared that the variations in the sensitivity of bacteria, and the possibility of otherwise sensitive organisms developing resistant variants, made it essential that antibiotics should be used only for the treatment of specific infections and not for the treatment of clinical syndromes. If this was to be done there must be close collaboration between clinician and bacteriologist. Possible toxic manifestations of antibiotics and chemotherapeutic agents must always be remembered: allergic reactions, blood dyscrasias, and secondary effects resulting from elimination of normal flora were among the most important. Local irritation or necrosis was especially important in ophthalmology and might be assessed by the effect of antibiotics on tissue cultures. Drug resistance could sometimes be overcome or prevented by combining two chemotherapeutic agents. Synergetic effect might be obtained by using two bactericidal substances; there was a possibility, however, of antagonistic action when a bactericidal drug was used in combination with a bacteriostatic substance.

Professor ARNOLD SORSBY pointed out that the eye was pharmacologically a double organ. Diseases of the external eye responded to antibiotics in the same way as diseases of other tissues of the body. However, drugs given systemically were prevented by the blood–aqueous barrier from entering the intraocular fluids and cornea freely. Consequently the treatment of infections of the interior of the globe and cornea presented special problems. Small concentrations of antibiotics could be found in the aqueous after enormous systemic doses, but only penicillin was sufficiently non-toxic to allow such dosage. Subconjunctival injection was required if high intraocular concentration was to be obtained. Antibiotics suitable for this method of administration were penicillin and streptomycin in solution and chloramphenicol in micronized suspension. Of the

relatively non-toxic members of the sulphonamides, sulphamerazine was the most likely to be effective in intraocular infection, as it penetrated the blood–aqueous barrier the most readily.

Mr. DEREK AINSLIE then described a hitherto little-used antibiotic, polymyxin, the particular property of which was its powerful bactericidal effect against the Gram-negative bacillary organisms. He had found it suitable for subconjunctival injection, and when given in this way it was effective against both experimental and clinical infections of the cornea due to the destructive *Ps. pyocyanea.*

In the discussion which followed, Dr. G. SAUBERMANN (Switzerland) said that intraocular infections could be treated with aureomycin given intravenously. Dr. H. MILLER (France) had found that the application of antibiotics to a scarified area of the sclera induced intraocular penetration.

Nova et Vetera

PELICANS AND PINCERS

Old Instruments Used for Extracting Teeth. By Sir Frank Colyer, K.B.E., LL.D., F.R.C.S. (Pp. 245; 283 figures. 42s.) London and New York: Staples Press. 1952.

In Britain a separate dental qualification has existed for less than a century; before that teeth were extracted by surgeons, apothecaries, barbers, and quacks, and perhaps even by some physicians. The evolution of the instruments used for the extraction of teeth should therefore interest not only the dental but all branches of the medical profession, and their curiosity will be amply satisfied by the perusal of Sir Frank Colyer's book. The name of the author is sufficient guarantee of the accuracy and thoroughness of the historical research. The book is based on the Wallis memorial lecture delivered in 1938, and the unavoidable delay in publication has enabled much new matter to be added, so that, as now issued, it must be the most complete available account of all the instruments used for dental extraction from the dawn of history until modern times.

We are told there is no evidence that there were any special dental instruments known to the Egyptians, and that extraction of teeth, though practised by the Greeks, was by them confined chiefly to loose teeth, so that one of their writers commented: "As to the pincers for pulling out teeth, anyone can handle them." Yet we have no reliable illustration of dental instruments until the eleventh century in the work of Albucasis. A gap of three centuries then ensued, when Arcoli, in a commentary on a book by Rhazes, also described and illustrated such instruments. From the sixteenth century onwards we meet with many books describing a varied assortment of instruments which can be classed as pelicans, keys, elevators, and forceps, and it is under these headings that Sir Frank has described the multitude of weird and wonderful devices used by ingenious and sometimes misguided inventors. To the uninitiated it would appear that some of the instruments were too cumbrous and complicated, and we felt sympathetic with the remarks of Serre, who wrote of one curious instrument: "Such an invention could only originate from an author to whom the art was not perfectly known. . . . I know of only one dentist who has this instrument and I believe he has it only for exhibition to the ignorant." Let the reader study attentively the numerous well-produced illustrations and judge for himself if he could have told what was the purpose of the instruments pictured in Figs. 258 and 273. Probably everyone will agree with the last paragraph in the book, which reads: "This survey of the instruments used in olden days for the extraction of teeth must leave us with the grateful feeling that the use of anaesthetics and more scientifically constructed appliances has rendered the operation a less terrifying procedure."

The reader will note that many of the illustrations are from instruments in the Odontological Section of the Museum of the Royal College of Surgeons, a unique collection which should be better known than it is. Let no one be deterred by the fact that the Colyer Museum is housed in a rather remote underground part of the College. It should be visited by every dentist and everyone interested in the history of this branch of surgery.

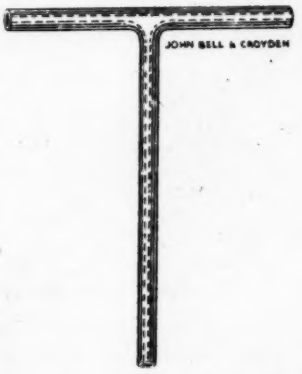
The most interesting fact in the book occurs on p. 57, where we learn that the oldest dental instrument in this country is housed, of all places, in the Royal College of Physicians. Is this a relic of a surgical past?

V. ZACHARY COPE.

Preparations and Appliances

THE LONG T-TUBE

Mr. RODNEY MAINGOT, surgeon, Royal Free Hospital, writes: The long T-tube, as illustrated, is a modification of the Kehr and the Cattell tubes which are now so often used in the surgery of the bile ducts. The tube is made of pure latex rubber, has a diameter of 10 English gauge (18 French gauge), is strong and durable, and is moulded into a single unit in order to avoid any weakness or defect at the point of union of the two limbs. The cross-limb measures 12 in. (30 cm.), whilst the other limb (which is led to the surface of the abdomen for drainage purposes at the end of the operation) is 13 in. (32.5 cm.) in length.



This T-tube may be employed with gratifying results after exploration of the bile ducts for choledocholithiasis; reconstructive operations upon the biliary passages for simple or malignant strictures; transduodenal choledochostomy for impacted stone in the ampulla, papillitis, fibrosis of the sphincter of Oddi, or excision of a small neoplasm of the papilla of Vater; and graduated dilatation of the lower reaches of the duct in cases of relapsing or recurrent pancreatitis. It has also proved most helpful in some difficult and hazardous gastro-duodenal resections for large, oedematous, and deeply penetrating posterior-wall duodenal ulcers.

For the common case of choledochostomy for stone in the bile ducts, after the ducts have been cleared of calculi and debris and after the ampullary region has been adequately dilated with flexible Bakes dilators, it is customary to trim the short arm of the T-tube to the requisite size so that one portion lies in the common hepatic duct whilst the other portion lies in the common bile duct. After the opening in the choledochus has been closed in a watertight fashion the long arm of the T-tube is led to the exterior.

For most of the other lesions which have been mentioned, it is advisable to pass one portion of the short arm of the T-tube downward, through the choledochostomy opening, into the duodenum, whilst the other portion above the "join" is pruned down so that it can be readily placed in the common hepatic duct.

So far as can be ascertained, there is little, if any, reflux of duodenal contents into the biliary tree, whilst the advantages of employing this indwelling tube, for the types of cases I have described, are considerable.

After many trials and adaptations this T-tube, as now made by John Bell & Croyden, Wigmore Street, London, W.1, has proved of inestimable value in the surgery of the bile ducts, and also in the occasional case of partial gastrectomy for the large callous penetrating ulcer of the duodenum.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Apnoea in Anaesthesia

SIR,—In your leading article (*Journal*, April 18, p. 875) on apnoea in anaesthesia the sting lies in the tail. The final sentence reads : "Further, the differential pressure changes occurring in the lungs and respiratory tract should not be such as to cause disturbance to the cardiovascular system." I believe that many physiologists will be surprised to learn that positive pressure ventilations can be carried out at all without causing some disturbance in the cardiovascular system. The disturbance is small, no doubt, usually well tolerated, and more than compensated by the other advantages of quiet, full ventilation which perhaps can in the particular circumstances be secured only by positive pressure inflation.

Nevertheless there are still anaesthetists so old-fashioned as to believe that in certain cases the unavoidable slight disturbance of cardiovascular function consequent upon positive pressure inflation may become of critical importance. I believe that there are critically ill patients who do better if they are allowed to breathe for themselves, and it seems to me that it is the anaesthetist's business to balance the risks and pick these cases out. One often has to do a little harm in order to achieve more good, but it seems wrong to lose sight of the fact that the "little harm" is a real thing.—I am, etc.,

Newcastle-upon-Tyne. E. A. PASK.

Modern Anaesthesia in Prostatic Surgery

SIR,—I was most interested in the letter by Dr. H. W. Loftus Dale and his colleagues on the use of spinal plus regional analgesia for prostatectomy (March 28, p. 727). I have been using this method for several years and my experience covers over 200 cases, including many elderly and poor-risk cases.

The technique I use is briefly as follows. Premedication, morphine ¼–½ gr. (8–11 mg.), atropine 1/100 gr. (0.65 mg.), given one hour before operation. Frequently quinalbarbitone sodium 1½ gr. (0.1 g.) is given before commencing the anaesthetic. Ephedrine-procaine 1 ml. solution is injected intraspinously; then, after administering a low spinal anaesthetic using heavy cinchocaine, a field block of the lower abdomen is performed. The anaesthetic solution consists of 200 ml. of 1 in 2,000 amethocaine hydrochloride solution to which 0.5 ml. 1 in 1,000 adrenaline and one ampoule of hyaluronidase are added. The ilio-inguinal and ilio-hypogastric nerves are blocked on each side medial to the anterior superior iliac spine, and a bilateral lower rectus sheath block is carried out. Anaesthetic solution is then infiltrated along the midline from umbilicus to pubis. Finally, a few millilitres of solution are infiltrated into the neck of the scrotum on each side of the division of the vasa. The procedure is a little more difficult in obese patients, but the use of a longer needle with, perhaps, a little more anaesthetic solution will usually provide a satisfactory result.

This form of anaesthesia produces an excellent operating field for the surgeon. There is minimal respiratory muscle paralysis, so that the patient tolerates the Trendelenburg position very well. The fall in blood pressure is rarely very great and is usually adequately controlled by one or two small intramuscular injections of a vasopressor. In our experience reactionary haemorrhage and clot retention are uncommon. I would like to endorse Dr. Loftus Dale's opinion of the value of this method of anaesthesia for prostatectomy.—I am, etc.,

Salford. MARK SWERDLOW.

Cerebrospinal Fluid Pressure

SIR,—I was interested in Dr. David Bowsher's article (*Journal*, April 18, p. 863) on the C.S.F. pressure, in which there are many important points which must be challenged.

Dr. Bowsher says, "Fluids are virtually incompressible, and so do not obey Boyle's law." For "fluid" surely is here meant "liquid"; according to the *Shorter Oxford English Dictionary*, fluid is "a general term including both gaseous and liquid substances consisting of particles that move freely among themselves so as to give way before the slightest pressure," whereas a liquid is "a material substance in that condition in which its particles move freely over each other (so that its masses have no determinate shape) but do not tend to separate as do those of a gas. Fluids are divided into liquids, which are incompletely elastic, and gases, which are completely so." The use of the words fluid and liquid as synonymous is a common mistake, but should not occur in a scientific statement. It follows from this that Boyle's law has no relevance to the argument, the law being that the volume of a gas varies inversely as the pressure. Although for practical purposes liquids may be considered incompressible, nevertheless under great pressure there is a slight diminution of volume, and up to pressures of 65 atmospheres the compression is proportional to the pressure. It follows that a closed rigid container may be filled to capacity under atmospheric pressure (that is, zero pressure if we choose to call it so for simplicity's sake), or it may be filled under any pressure chosen. In the example given (Fig. 1) extra liquid introduced into the cylinder will rise in the U-tube, by displacement, and will indicate by the height of its new level the pressure within the cylinder. A motor-car could not be raised by a hydraulic jack if pressure were not imparted to the liquid contents.

In Fig. 3 we are not informed of the units of the axes of the graph, but it is clear from visual measurements that there is a considerable alteration of pressure between A and B, whatever units of pressure may be employed. Surely the pressure within the elastic tube necessary to change its cross-section from ellipse to circle will depend also on forces acting outside the tube; if we are dealing with a vein in the subarachnoid space, it will depend on the C.S.F. pressure around the vein, tending to collapse it, as well as on its elasticity (or rigidity) and the intravenous pressure. Applying his argument, Dr. Bowsher states that a volume increase in the tube bringing it from an elliptical to a circular cross-section will cause no increase of pressure—although his graph shows there is an increase of pressure which he contends is small—but will displace liquid into the U-tube, which elevates the height, H, by the additional h_1. This h_1 is clearly the manometric increase of pressure; his manometer is not only measuring volume, it measures pressure, which he seems to ignore.

"The dura is inelastic." This statement is incorrect, as anyone who has watched a craniotomy in a case of high intracranial pressure can observe for himself. When the bone flap is raised, the dura mater will immediately stretch slightly but unequivocally. And if before the dura mater is opened the bone flap is replaced it will be found to be "riding" in its defect and will need force to be rendered flush with the surrounding cranium, in its former position.

"Partially collapsed veins can be changed from elliptical to circular cross-section without increase in pressure." This misleading statement has been dealt with above, and is disproved by the published graph Fig 3. And if an increase in intravenous pressure does not change them, what does ?

Dr. Bowsher later states that "it has hitherto been held" that the rise in the pressure of the C.S.F. (presumably in the lumbar theca) on abdominal compression is due to failure of C.S.F. to be absorbed while its secretion continues. I do not know who has held this view, but it is certainly neither held nor taught in knowledgeable neurological or neurosurgical circles. It has been taught for many years that such a rise is due to the increase of pressure in abdominal veins being communicated to the vertebral plexus of veins and thereby the lumbar C.S.F. In Queckenstedt's test, the compression of the jugular veins leads to distension of the intracranial veins, as Dr. Bowsher correctly states, and they distend (or become circular) because the pressure within them rises inevitably; and there is some displacement of C.S.F. into the spinal theca. The pressure within the cranium rises, and can be measured by a manometer attached to a needle in the ventricle, and the pressure rise can also be measured by lumbar manometry. Dr. Bowsher here puts the word pressure in inverted commas; does he not believe he is measuring pressure with his manometer ? Of course, the quantity of liquid filling his manometer vitiates to some extent the actual figure of the

pressure; his reading will be slightly less than the actual pressure present before he connected up his manometer. And to render this error as small as possible all spinal manometers should be constructed with tubing of as fine a calibre as is practicable.

"The dura must therefore be looked upon as adhering to the cranium and vertebral canal." Yes, the dura (except for its great partitions) is adherent to the inner surface of the skull; that is an anatomical fact, and for that reason only the dura covering the brain in the intact skull can be considered inelastic. But the dura is not adherent to the spinal canal; that also is an anatomical fact and cannot "be looked upon" as anything else. Weed and others, to whom Dr. Bowsher refers, realized this, and on the presence of this extradural spinal space containing veins and fatty areolar tissue rests their explanation for their various "tilting" experiments to which Dr. Bowsher refers. Indeed, in certain positions this spinal extradural space is under negative, that is, less than atmospheric, pressure. Were the dura not loose in the spinal canal displacement of C.S.F. from the cranium could only occur at the expense of spinal venous blood.

Dr. Bowsher makes other comments concerning the maintenance of the normal C.S.F. pressure, a subject much too large to be dealt with by correspondence, and I have already trespassed excessively on your valuable space. May I suggest that he refers to a summary of this subject in the section on the nervous system in *Recent Advances in Surgery* (Churchill, 1948), where the more important references may be found. Finally, in his summary Dr. Bowsher states that "there has been a fundamental misconception with regard to spinal manometry": I suggest that the misconception lies with Dr. Bowsher.—I am, etc.,

London, E.1. D. W. C. NORTHFIELD.

SIR,—How comes Dr. David Bowsher to ignore in his article, "The Cerebrospinal Fluid Pressure" (*Journal*, April 18, p. 863), the work of the late Sir Leonard Hill on this subject,[1] the correctness of which, as I have stressed,[2] is verified clinically by observation of the retinal venous pressure response at the disk?—I am, etc.,

Nottingham. THOMSON HENDERSON.

REFERENCES

1 *The Physiology and Pathology of the Cerebral Circulation*, 1896. London.
2 *Principles of Ophthalmology*, 1950. London.

The Training of Physiotherapists

SIR,—A certain prominence has been given lately in medical journals to the training of physiotherapists, and we feel that certain points ought to be clarified for the medical public. Physiotherapists in this country belong to three groups: (1) the Physiotherapists Association, (2) the Faculty of Physiotherapists, and (3) the Chartered Society of Physiotherapy. The Cope Report, drawn up by a committee of nine members, six of whom were in active association with the Chartered Society, whereas the other two bodies were not represented, recommended to hospital authorities to employ exclusively members of the Chartered Society, and the first circulars of the Ministry of Health were drawn in this spirit. The injustice of this Report, however, has been rapidly realized, and the Minister of Health stated in Parliament on March 19 that the Cope Report would not be implemented, and that he would further withdraw the temporary instructions in the Ministry circular referring to the employment of chartered physiotherapists, and make new regulations fair to all associations concerned.

We are at a loss to understand this tendency of the Chartered Society to monopolize physical treatment in this country. Apart from the fact that it goes against the liberal principles that dominate medical work, nothing has demonstrated the superiority of the members of the Chartered Society over those of the other associations of physical treatment practitioners. We must emphasize that hospitals employing members of the Physiotherapists Association and the Faculty of Physiotherapists are perfectly satisfied that the training of members of the Association and the Faculty is not inferior to that of the Chartered Society.

We are astonished at the boosting of the Chartered Society training in the letter by the president and vice-chairman of the council of that society (*Journal*, March 14, p. 615). The "schools" to which he refers are neither owned nor controlled by the Chartered Society, but are part of State hospitals. Thus the Chartered Society is using publicly owned and publicly maintained hospital facilities to bolster its monopolies. This, by the way, is an anomaly which undoubtedly will be corrected by Parliament. The education plan formulated by the Physiotherapists Association, and supported by education authorities, experienced teachers, and the medical profession, provides for the co-operation of the technical colleges and teaching hospitals. Physiotherapy training schools should be a part of a university and the physiotherapy qualification should be a recognized university diploma. The present standard of the Chartered Society, on whatever level it is assessed, is parochial compared to the real aim of producing a physiotherapist who can take his place as an accepted member of a medical team, receiving alike the support of the medical profession and the confidence of the public.—We are, etc.,

A. P. CAWADIAS, President.
S. S. KNIGHT, General Secretary.

The Physiotherapists Association, London, W.1.

The Metric System

SIR,—I think Dr. J. W. Shackle (*Journal*, April 18, p. 887) has confused the origins of the ml. and c.cm. The litre, as now defined, has no relationship to the metre and is not based on any linear measurement at all. Hence the thousandth part of a litre is not a cubic centimetre. The fact that the new litre has a volume of 1,000.027 c.cm. is a tribute to the skill of our forebears, and means that for practical purposes the thousandth part of the old litre (c.cm.) and new litre (ml.) can be regarded as identical. There is one volume used in medicine, however—namely, that of the haemocytometer chamber—which is still based strictly on a linear measurement. Haematologists are correct in using the term cubic millimetre, and would be wrong to speak of a "millimil."

I think Dr. Shackle may be unaware of the historical basis of all this, and would respectfully refer him to an excellent article on it by Dr. J. M. Hamill.[1]

Dr. Shackle rightly mentions the danger of the misplaced dot. May I remind your readers that a misplaced "squiggle" on the drachm sign is also dangerous? There are many published examples of overdosage from this.—I am, etc.,

Enfield. C. ALLAN BIRCH.

REFERENCE

1 *British Medical Journal*, 1947, 1, 460.

SIR,—So far, no serious arguments have been made against the introduction of the metric system into medicine. The latest one, advocated by Dr. R. A. C. Herron (*Journal*, April 25, p. 938), seems utterly frivolous. If I understand him correctly, the metric system should not be used because "for some reason of habitual usage" no one in Zurich would understand what is meant by 0.5 mg. or half a milligram. Apparently it is necessary to say or write 0.0005 g. If milligrammes were regularly used for small doses, fractions of any sort would only occasionally be used, for, as near as makes no difference, 1 mg. = 1/60 gr., 0.5 mg. = 1/120 gr., and doses smaller than 1/120 gr. are seldom used. If very small doses are employed then micrograms (μg.) are very convenient—e.g., 50 μg. of vitamin B_{12} (= 0.05 mg., or gr. 1/1200).

Dr. John Primrose (*Journal*, April 4, p. 782) says he uses the metric system for his scientific work but prefers to "prescribe opiates in vulgar fractions of a grain." Why is morphine gr. ¼ more convenient than 15 mg. of morphine? No one would dream of prescribing pethidine in the old system. It is purely a matter of what one is used to, and there is a lot to be said for getting rid of these fractions of a grain, which sometimes are absurdly small, as the dose of digitaline, which is gr. 1/600 in the old system.

A great deal has been written about the allegedly cumbersome numbers used in the metric system. For instance, Dr. C. Langton Hewer (*Journal*, February 21, p. 450) quotes the pre-anaesthetic dose of paraldehyde as 3.55 ml. per 6.35 kg., but the approximate metric equivalent is 0.5 ml. per kilogram, which has already been pointed out by Professor W. C. W. Nixon and Mr. T. D. Whittet (*Journal*, March 14, p. 619). It cannot be too strongly emphasized that exact equivalents are not required. Doses in the old system are *adjusted* to the convenience of the system, and in general "round numbers" and "simple fractions" are employed—for example, 5 gr., 30 gr., ¼ gr., 1/100 gr., etc. If doses now ordinarily expressed in the metric system are accurately changed into the old system, equally cumbersome figures are obtained—for example, 1 g.=15 2/5 gr. and 1 ml.=16 9/10 minims. No one has used this argument against using the old system, but it equally applies.

There is no doubt that the metric system is simpler and far less cumbersome than the old system. All medical students would welcome it, and its introduction into medicine would bring our subject into line with all the other sciences all over the world. I have vivid memories of my dismay in having to learn and understand the apothecaries' system after having used and easily understood the metric system for years while doing science at school and at the university. British and American textbooks and journals are extensively read in other countries, and the old system of dosage often employed must be incomprehensible to many readers, even when they have a perfect knowledge of English.—I am, etc.,

Thornton Heath. G. P. BAKER.

Iron Therapy

SIR,—I have followed the correspondence on iron therapy with interest and await the results of the investigations of Professor P. Larizza and Dr. S. Ventura (*Journal*, April 18, p. 885).

As a general practitioner, my chief worry has always been the tolerability of iron compounds. I decided to carry out a clinical test of ferrous gluconate, the results of which were published in February this year.[1] I found that a ferrous gluconate preparation gave most satisfactory results. Not only is it an adequate substitute for ferrous sulphate, but causes no digestive disturbances whatsoever. I would draw this new preparation to the attention of all general practitioners who have been bothered, as I have been bothered, by the inability of a large proportion of secondary anaemias to tolerate ferrous sulphate and other compounds.

To quote your Italian correspondents, it may be incautious to infer that ferrous gluconate used by itself is a more efficient haematinic than ferrous sulphate, but I am prepared to assert from the results I have obtained that it is every bit as good, and its easy tolerance and absence of side-effects make it by far the most useful preparation that we have available to-day.—I am, etc.,

Cardiff. W. MERFYN JONES.

REFERENCE

[1] *Practitioner*, 1953, **170**, 185.

Blood Grouping and Cancer of Stomach

SIR,—Professor Ian Aird and his colleagues (*Journal*, April 11, p. 799) appear to have shown that persons of blood group A have a greater susceptibility to cancer of the stomach than have those of blood group O. Such studies of varying susceptibility to disease should be vigorously pursued because information of immediate practical value may be obtained. For instance, Chevallier and Desoille[1] showed that workers who handle benzene and are of blood group O are much more susceptible to ill-effects than are those of blood group A, while those of blood groups B and AB have a susceptibility intermediate between these two groups. Indeed, these authors go so far as to suggest that the possession of blood group A should be essential for all workers in benzene. Unfortunately, this work has not, so far as I can discover, been pursued either in France or elsewhere. Of less immediate practical importance is the apparent fact that more leukaemics are of blood group A than of blood group O, while haemorrhagic diseases seem to be most common among people of group O.

Unfortunately the published work has dealt with relatively small series of cases, but if the workers and funds were available it should not be difficult to collect a large series of observations from the records of the hospitals of this country.—I am, etc.,

London, W.1. A. PINEY.

REFERENCE

[1] *Sang.* 1947, **18**, 126.

Respiratory Function

SIR,—Dr. K. W. Donald, in Part I of his article on the assessment of respiratory function (*Journal*, February 21, p. 415), remarks that it is still not known why a person should be uncomfortable when exercise causes him to ventilate about half the air that he can shift at rest without distress, by voluntary hyperventilation.

Could the answer be that during exercise the cardiac output is greatly increased from both sides of the heart and the pulmonary vascular bed becomes dilated and even new channels opened up, with a great increase in the quantity of blood in the lungs? This will prevent full alveolar expansion and ventilation, a condition somewhat analogous to the pulmonary congestion of mitral stenosis. Has the blood volume of the lungs during exercise been compared with that during voluntary hyperventilation?

Secondly, during exercise an oxygen debt is built up and there is a temporary anoxaemia not present during voluntary hyperventilation. This will have an additional effect of increasing the dyspnoea.—We are, etc.,

GEOFFREY FFRENCH.

Champion Reefs, S. India. B. N. KRISHNAMURTHY.

Erythrocyte Sedimentation Rate Irregularities

SIR,—The recent papers on erythrocyte sedimentation rate irregularities by Gilmour and Sykes[1]; Goldberg, Glynn, and Bywaters[2]; Goldberg and Conway[3]; and Alexander[4] prompt me to report the findings of my own investigations, which were begun in 1949.

One of the disadvantages of the Westergren method is the difficulty of obtaining at the bedside the exact degree of dilution of blood with sodium citrate solution. It was thought that such dilution errors could be overcome by the use of heparin (solid) as an anticoagulant. Very irregular E.S.R.s were observed by this method—one patient with an E.S.R. of 60 mm. appeared to have an E.S.R. of 5 mm. a week later. It seemed that the change of anticoagulant might be the cause of these anomalous readings, and so the matter was investigated. It was found that irregular (low) one-hour readings were associated with the use of solid anticoagulants such as heparin and the oxalate mixture of Heller and Paul.[5] These irregularities were found to be caused by an excessive prolongation of the aggregation phase of sedimentation (Cutler[6]) due to an inhibition of rouleaux formation. This inhibition occurred more frequently in deoxygenated blood, and it was found that, if blood known to have a high E.S.R. was equilibrated with carbon dioxide, rouleaux formation was so inhibited that the one-hour E.S.R. reading was reduced to normal limits. This inhibition appears to be a metastable state, for after an interval of 30–50 minutes the *whole column* of blood suddenly becomes coarsely granular (intense rouleaux formation) and very rapid sedimentation then occurs. If this inhibition lasts over 45 minutes and the E.S.R. is read at one hour a falsely low reading will result. This metastable state might be considered to be a hysteresis phenomenon. Such prolonged inhibition of rouleaux formation could not be obtained with blood using a liquid anticoagulant (3.8% sodium citrate solution). E.S.R. irregularities with blood using a solid anticoagulant were eliminated by diluting this blood with 3.8% sodium citrate solution.

This phenomenon appears to be the same as that originally observed by Lundgren[7] in hirudinized blood. The effect of CO_2 and O_2 on the E.S.R. has in the past been considered

to be unimportant, for, though CO_2 was found to decrease and O_2 to increase the E.S.R., the changes were found to be small (Leendertz[8] and Ito[9]). These findings were based on experiments using liquid anticoagulant—3.8% sodium citrate solution as originally used by Fåhraeus.[10] When the solid oxalate mixture of Heller and Paul began to be employed for the determination of the E.S.R. by the Wintrobe method, it appears that previous work was not repeated to ascertain whether findings related to liquid anticoagulants also applied to solid anticoagulants.

Full details of this work have been submitted for publication.—I am, etc.,

McD. DUXBURY.

REFERENCES

1 *British Medical Journal*, 1951, 2, 1496.
2 Ibid., 1952, 1, 202.
3 Ibid., 1952, 2, 315.
4 Ibid., 1953, 1, 433.
5 *J. Lab. clin. Med.*, 1934, 19, 777.
6 *Amer. Rev. Tuberc.*, 1929, 19, 544.
7 *Acta med. scand.*, 1927, 67, 63.
8 *Dtsch. Arch. klin. Med.*, 1921, 137, 234.
9 *Tokohu J. exp. Med.*, 1924, 5, 139.
10 *Acta med. scand.*, 1921, 55, 1.

Subserous Duodenal Haematoma

SIR,—In his medical memorandum (*Journal*, March 28, p. 712) Mr. D. I. Stirk records a case of subserous duodenal haematoma resulting from a "non-penetrating and apparently trivial injury." I should like to record a similar case in which the injury was sustained in an identical manner.

A child aged 6 years was admitted to hospital four days after a blow in the left hypochondrium from the handlebars of his bicycle. After the injury he continued his journey home, but subsequently complained of recurrent bouts of upper abdominal pain, followed in 24 hours by anorexia and vomiting of bile-stained fluid. An enema had been given on the second day with a good result. On admission to hospital the child was found to be slightly pyrexial, had a dry tongue, and abdominal examination revealed rigidity of the left side, maximum in the left hypochondrium. Rupture of the spleen was diagnosed and laparotomy advised. This showed absence of any free fluid in the peritoneal cavity, but revealed a large tense black sausage-shaped swelling about 6 in. (15 cm.) in length in the region of the upper jejunum. This was thought to be gangrenous bowel, but immediately this was touched the tense lesion burst and extruded a quantity of black blood clots. The lesion was then discovered to have been a subserous haematoma. The first 15 cm. of the jejunum and its mesentery appeared to be grossly disorganized and was resected. An end-to-end anastomosis at the duodeno-jejunal flexure was done. The child made an uneventful recovery. Examination of the specimen showed disorganization of most of the tissues by blood clot, but the actual bowel mucosa appeared to be healthy.

It is of interest to note that this injury occurred in the same fashion as the case reported by Mr. Stirk—that is, by a child riding a bicycle. There were no external signs of bruising and the injury at first seemed trivial, its effects being seen only after some hours. This lesion is quite distinct from a traumatic rupture of the mesentery with free intraperitoneal haemorrhage, and its signs are delayed in onset. This is a point well to be borne in mind when one remembers that these types of accidents commonly find their way to casualty departments and are often first seen by a junior member of the hospital staff.—I am, etc.,

Ipswich. C. I. COOLING.

A Paper Not Read

SIR,—Several most serious issues for the medical profession as a whole are involved in the case of *Crawford* v. *Charing Cross Hospital*. Having attended the whole proceedings and heard the judgment, the features which cause the greatest concern are the following:

Nothing was done or left undone which in any way departed from widely accepted practice at that time, practice which had indeed never produced a palsy throughout the long professional career of the anaesthetist.

The angle of abduction was within the right angle—to quote the judgment: "an angle of 80 degrees or thereabouts."

Mr. Justice Gerrard expressed the view that he did not think the problem of negligence or no negligence turned upon current practice. He admitted the advantages of abduction of the arm for good blood flow and general observation.

Mr. Ewing[1] had warned against the dangers of abduction. The anaesthetist, never having met a brachial palsy and therefore considering his precautions adequate, did not read the article in spite of being aware of its existence. To quote the judgment: "Nice questions might arise as to how far a medical man could excuse his ignorance of a technical development that he had not met in his reading of his professional journals." It was the anaesthetist's "duty to follow up the writings on a subject which concerned him closely." "I think it was regrettable slackness that left Dr. X in ignorance of the opinions of distinguished men on an important subject so closely affecting his own work at the time he came to administer the drip to the plaintiff."

Does written advice transcend in importance long practice and experience in guiding our actions?

We practise our profession at first largely as we have learnt it from our teachers, and improve as the years go by from our own experience combined with discussion and selective reading from the vast modern output of literature. Current practice is always lagging—and often how rightly so—well behind the pioneers of new methods. This dangerous precedent that such practice can become negligent within a few months of a new paper is one which must be fought in the Court of Appeal and even, if need be, in the House of Lords.—I am, etc.,

London, W.1. MICHAEL ASHBY.

REFERENCE

1 *Lancet*, 1950, 1, 99.

Dosage of Stilboestrol

SIR,—With reference to recent correspondence regarding the dose of stilboestrol the following observations may be pertinent so far as prostatic cancer is concerned.

In treating this condition the optimum dosage is basically determined by the amount of oestrogen required to control or retard the progress of the growth, qualified by there being no unreasonable risk that this quantity will evoke dangerous side-effects or complications. With regard to the former, objective evidence of tumour control can only be directly adduced from serial histological examination in cases where repeated biopsy is practicable during treatment. At the same time, owing to known variations in the natural course of the untreated disease, indirect information afforded by a study of the survival periods of patients receiving oestrogens will only establish the efficacy of a particular dosage if a large series of cases is reviewed.

Both these aspects have received attention in a recent survey of a personal series of 150 consecutive cases of histologically proved prostatic cancer treated with oestrogens. These cases, extending over the period 1942–52, have been divided into three groups receiving respectively a sustained dosage of 1–5 mg., 15–30 mg. and (more recently) 100 mg. stilboestrol daily. Repeated histological examination of the growth on two or more occasions during treatment was possible in 33 patients,[1] and evidence was obtained to show that, after an initial favourable response to small and large doses alike, many tumours ultimately became oestrogen-resistant. In some instances, however, a tumour which had apparently become resistant showed further evidence of response to oestrogens when the dose of stilboestrol was increased, and a distinction was thus apparent between growths showing a relative and an absolute loss of sensitivity. Although in no case was complete regression of a tumour achieved, it seemed likely that a failure to obtain prolonged retardation of growth in some represented the effect of inadequate dosage rather than a spontaneous increase of biological activity. This view is supported by a study of the survival periods of the entire series of cases, in that the average duration (making appropriate allowance for the comparatively recent introduction of the highest dosage) seems to be significantly increased in those receiving larger amounts of stilboestrol.

It would appear, therefore, from the direct and indirect evidence afforded by these methods of investigation, that,

so far as tumour activity is concerned, sustained treatment with at least 100 mg. daily is advisable. It is frequently alleged that prolonged dosage of this magnitude is more liable to evoke troublesome nausea and vomiting than when smaller quantities are prescribed. In my experience, however, this has not proved to be the case, the few examples encountered having been treated satisfactorily either by subcutaneous oestrogen implants of comparable strength or by supplementary castration. More recently, in instances where the primary growth has responded well to oestrogens but in which metastatic activity has subsequently increased despite sustained therapy, a few advanced cases have been treated by bilateral adrenalectomy and cortisone substitution with gratifying immediate results.—I am, etc.,

London, W.1. J. D. FERGUSSON.

REFERENCE

[1] Fergusson, J. D., and Franks, L. M. (1953). *Brit. J. Surg.*, 40, 422.

Radioactive Phosphorus in Treatment of Menorrhagia

SIR,—We do not share Mr. D. K. Sambrook's cheerful opinion (*Journal*, April 18, p. 883) of *x* rays as a method of controlling simple uterine bleeding. In fact, our deep dissatisfaction with irradiation of the ovaries is based on studies of over 200 women who suffered from the side-effects of castration. For instance, the incidence of serious and persistent menopausal flushing and sweating is 50%, three times the normal, while the sudden onset of sexual anaesthesia or, at a later date, of senile vaginal changes must surely be considered as the cost of irradiation.[1] No doubt Mr. Sambrook, like ourselves, has to treat the side-effects of irradiation with oestrogens, but I am sure he will admit that it is a great nuisance to his patients and to himself, especially if his treatment creates a new and worrying symptom, post-menopausal bleeding. Our experiments with P^{32} were carried out in the hope that bleeding might be controlled without the effects of ovarian irradiation. We do not yet know if certain patients might resume normal menstruation after P^{32}, nor do we know how many patients might reach the normal menopause.

We freely admit Mr. Sambrook's point that P^{32} cauterization of the endometrium does not attack the cause of the bleeding. In fact, in the vast majority of patients we do not know the cause, although we have discovered the wisdom of avoiding vague phrases such as "unbalanced production of oestrin" and "hyperoestrinism." The Birmingham students have a habit of asking us what we mean by such phrases. Both Mr. Sambrook and ourselves are recommending damage or destruction as therapy; we apply a β-ray "cautery" to the endometrium, he recommends *x* rays to the ovaries. We disagree with Mr. Sambrook in that we believe the ovaries are of importance at the menopause. It remains to be seen if there are ill-effects and dangers associated with irradiation of the uterus with P^{32}. Lastly, we wish to state that our report was a preliminary one. We do not know if endometrial "cautery" by β-rays will prove itself as an effective therapeutic agent in menorrhagia.—We are, etc.,

HUGH C. MCLAREN.
J. C. HEATH.
A. QUINTON.

Birmingham.

REFERENCE

[1] *British Medical Journal*, 1950, 2, 76.

Nikethamide by Mouth

SIR,—Unfortunately, it is letters like the one written by Dr. J. V. Cope (*Journal*, April 18, p. 885) that tend to make us "qualified quacks" in the eyes of specialists, hospital staff, and newly qualified doctors. It makes it difficult for G.P.s to obtain clinical assistantships, and will further remove us from scientific and accurate work demanded in hospital. The letter is entirely uncritical in description and coloured by erroneous subjective observations. We teach our patients (wrongly) words like "cardiac debility" and in time become so enchanted by this meaningless word that we now try to teach it to each other instead.

Let us forget "subclinical cardiac debility" (which is so easily cured by nikethamide) along with "symptomless avitaminosis," "anaemia" when the haemoglobin is 98%, and "rheumatism of the knees" when the correct diagnosis is probably climacteric arthritis.

It is not the N.H.S. that has lowered our status as G.P.s but merely the fact that we now allow a much larger proportion of our patients to seek hospital advice and thus expose—I tried to avoid the phrase—the skeletons in our cupboards.—I am, etc.,

Luton. H. JARVIS.

SIR,—May I endorse Dr. J. V. Cope's remarks on nikethamide by mouth and his appeal for further observations (*Journal*, April 18, p. 885), my own being frustrated by a shortage of cases of chronic bronchitis?

I was recently driven to prescribe nikethamide, 15 min. (0.9 ml.) orally in water, for severe paroxysmal dyspnoea in two advanced bronchitics with no clinical signs of heart failure. Both had already been treated with ephedrine, isoprenaline sulphate ("neo-epinine"), watery and oily adrenaline by injection, and "rybarvin" type inhalation. Both claim really dramatic relief and have been using it regularly for three months. This militates against the effect being purely psychological, together with the fact that I only imagined it to be a placebo myself and did not extol its virtue.

It is difficult to see why Dr. J. G. Macarthur (*Journal*, March 7, p. 547) did not start with usual dosages, though easy to appreciate that a patient in the throes of nausea and vomiting might report unfavourably or not very objectively on the agent which had caused it. Before estimating blood nikethamide levels and then consigning a possibly valuable paper and useful therapeutic agent to the dustbin, could he not also ask them how they react after a normal dose given orally—with appropriate controls, of course? This point has received somewhat cursory attention in the present paper, and, from what one can gather, will receive none at all in its sequel.

Whether this drug helps the patient is of rather more interest than its physiology.—I am, etc.,

Staines, Middlesex. J. A. SINDELL.

Treatment of Ringworm of the Scalp

SIR,—Dr. S. Cochrane Shanks (*Journal*, April 4, p. 780) has written a similar letter on a former occasion.[1] No one doubts that, under the ideal conditions to which he refers, the chances of permanent alopecia following *x*-ray epilation are virtually nil. It may be that the continued embarrassment of prescribing wigs for the victims of earlier decades results in the over-emphasis of this therapeutic tragedy.

Some doubt exists, however, regarding the choice between an anaesthetic and the restraining couch, and not all radiotherapists, it seems, are in agreement with Dr. Shanks. Beare and Cheeseman,[2] reporting on 1,004 cases of scalp ringworm, advocate the use of anaesthesia for children between 1 and 3 years, mental defectives, and obstreperous subjects. Even if one encounters a case of *M. canis* infection that is "sufficiently persistent to warrant epilation"—and I have yet to do so—it should not influence one against the simpler and normally successful treatment. Nor would I expect the radiotherapist to abandon his *x*-ray epilation because of his occasional failure. During the Newcastle epidemic there were 13 "failed *x*-ray cases" in 1949.[3]

Without quoting a single reference, Dr. W. A. Dewar (*Journal*, April 14, p. 780) claims that the majority of authorities are in favour of *x*-ray epilation for *M. canis* ringworm. In fact, the reverse is true, and it would be unfortunate if such an ill-founded assertion were to gain credence. The mycologists, Lewis and Hopper,[4] state:

"In several publications we have called attention to the tendency to spontaneous cure and to the success of local measures alone when tinea capitis is caused by *M. lanosum*." Muende[5] writes: "The fact that animal microsporum infections usually respond to such simple treatment should encourage one to conduct careful cultural examinations of infected hairs before resorting to the commoner techniques of *x*-ray and thallium epilation." I would also refer him to Duncan,[6] and Schwartz *et al.*[7]

Dr. Dewar considered that, to ensure against missed cases, routine Wood's lamp investigation should have been carried out at the schools involved in the investigation. The frequency of erythema reactions and also of coincident glabrous skin involvement as a means of diagnosing *M. canis* scalp infections renders this unnecessary.

Surely the experiment of waiving the school exclusion rule should be judged by the subsequent incidence of ringworm in the area concerned. Following on the cases reported up to March, 1952, three more cases occurred in March and two in May. All five came from different schools, at which they were of course allowed to continue attendance. From May, 1952, to April, 1953, not one case of *M. canis* ringworm has been reported in the County Borough of Newport.—I am, etc.,

Newport, Mon. BERNARD A. THOMAS.

REFERENCES

1 *British Medical Journal*, 1949, 2, 1351.
2 *Brit. J. Derm.*, 1951, 63, 165.
3 Annual Report of Principal S.M.O., Newcastle-upon-Tyne, 1949.
4 *An Introduction to Medical Mycology*, 1943, Year Book Publishers, Chicago.
5 *Modern Practice of Dermatology*, edited by G. B. Mitchell-Heggs, 1950, Butterworth's Medical Publications, London.
6 *British Medical Journal*, 1945, 2, 715.
7 *Publ. Hlth Bull. (Wash.)*, 1946, No. 294, 1.

Leprosy at Large

SIR,—The photographs I enclose were taken on March 23, 1953, two days after I found this case of leprosy in a rigor, hiding in a farm-labourer's cottage. The patient came to England a known and declared leper in 1947, and was for six months in a hospital for tropical diseases. She was discharged into our population to roam from home to home, hiding, as is the way of lepers, aided by her devoted husband. The condition of the husband, son, and home in the case that I now report was only what you would expect where the mother has no hands and virtually no feet. About a year ago another woman in this district with an unaccountable leonine frontal development was found by her

[*A. T. Schofield, A.R.P.S.*

[*A. T. Schofield, A.R.P.S.*

G.P. to have unsuspected leprosy. This letter is not intended to report the case clinically at this stage: it is intended to be a reminder of the existence in England of a disease one of the most striking social attributes of which is concealment. Its infectivity is low.

To admit lepers to England and not to follow them up may be followed by concealment, unnecessary suffering, crippling deformity, and thus a small additional burden to the community. This matter has already been vigorously represented by the district medical officer of health to the Ministry of Health and to his Member of Parliament without any alteration to the existing legislation concerning the notification and control of this disease.—I am etc.,

Steeple Ashton, Wilts. FITZ HAYTHORNTHWAITE.

*** The Public Health (Leprosy) Regulations, which provide for the notification of cases of leprosy direct to the Chief Medical Officer of the Ministry of Health, came into operation on June 22, 1951, several years after the discharge from hospital of the patient described by our correspondent. —ED., *B.M.J.*

West Memorial Lecture

SIR,—The students of the Welsh National School of Medicine have decided to establish a suitable memorial to the late Professor Cecil McLaren West, Professor of Anatomy in the school from 1927 until his untimely death in 1951. It is agreed that the memorial should take the form of a biennial lecture to be delivered in the medical school and designated the West Memorial Lecture.

To endow such a project it is desired to raise not less than £600, the interest on which can be used for the expenses of the lectureship. An appeal for contributions is addressed to all those who came into contact with Professor West. Members of the Medical School staff and past and present students have been approached, but this letter is addressed to all those members of the profession who would like to contribute towards the Memorial Fund. The closing date of the appeal is June 30, 1953. Any further particulars may be obtained from the chairman of the Memorial Committee at the undermentioned address, but all contributions should be sent to the Bursar, University College, Cathays Park, Cardiff. Cheques should be made payable to "The West Memorial Lecture Fund."

It is confidently hoped that the many friends of the late Professor West will help in establishing a worthy memorial to one whose life and work meant so much to so many.—We are, etc.,

JOHN H. HUGHES, Chairman. H. HUGHES.
JOHN PRYDE.

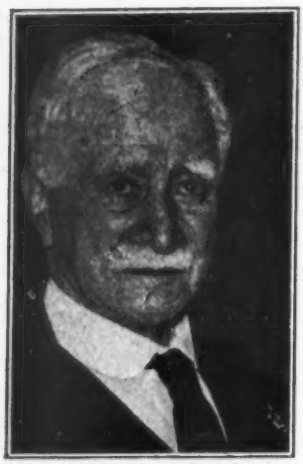
West Memorial Committee,
Medical Students' Club,
11-15, Howard Gardens,
Cardiff.

Obituary

Sir DAVID ROCYN JONES, C.B.E., M.B., D.P.H.

We record with regret the death on April 30 of Sir David Rocyn Jones at the age of 80. He was county medical officer of Monmouthshire for nearly forty years, and during the course of time he became one of the best-known and most popular men in the public life of South Wales and Monmouthshire.

David Thomas Rocyn Jones was born at Rhymney on November 16, 1872. His grandfather was famous in his day as a bone-setter in Cardiganshire. His father became a great friend of Hugh Owen Thomas, the pioneer of orthopaedic surgery in Liverpool, and David Rocyn Jones at one time thought of becoming an orthopaedic surgeon, as, in fact, his brother did. From Lewis's School, Pengam, he went on to the University College of South Wales at Cardiff, and later to University College, London. He continued the study of medicine at Edinburgh, where he graduated M.B., C.M. in 1897. Shortly after graduating he set up in general practice in Abertillery, having secured the appointment of surgeon to Powell's Tillery Collieries. Being also part-time medical officer of health of the town, he developed an interest in public health and took the D.P.H. of Oxford in 1904. Four years later—one of 97 applicants for the post—he became the first whole-time medical officer of health for Monmouthshire, the county of his birth. In 1908 preventive medicine was in its infancy, and Rocyn Jones built up a service which under his guidance went from strength to strength. Sufferers from tuberculosis had particular reason to be grateful to him, for in 1911 he was one of the founders of the Welsh National Memorial Association for the Prevention and Treatment of Tuberculosis.



[Barratts Photo Press, Ltd., London

David Rocyn Jones was a man of great geniality and wide interests, and he did not confine his activities to public health work. Very few medical officers of health can have played such an active part in public life as he did. Passionately fond of Rugby football, he was president of the Welsh Rugby Football Union at the time of his death, having been first elected to the Union in 1908. He saw the advance of Rugby football in Wales through many years of success, and at the time of his death he was regarded as "the grand old man" of Welsh Rugby. A leading figure in the affairs of the British Medical Association, he was chairman of the Monmouthshire Division in 1923 and president of the South Wales and Monmouthshire Branch in 1930–1. He was appointed a member of the consultative council of the Ministry of Health for Wales in 1919, and in later years he became a member of the Welsh Regional Hospital Board and chairman of the North Monmouthshire Hospital Management Committee. Controller of V.A.D.s for Monmouthshire and a member of the council of the Territorial Army Association, he was appointed surgeon-in-chief of the St. John Ambulance Brigade in Wales in 1936. He was also prominent in the Priory for Wales of the Order of St. John, and was a Knight of Grace of the Order. For many years he was a county magistrate, being formerly chairman of the Bedwellty division of magistrates. He was a staunch Congregationalist, being a member of the Monmouthshire Congregational Union. With all this public work to his credit, it was not surprising that Rocyn Jones received many honours. He was appointed C.B.E. in 1920 and Deputy-Lieutenant of Monmouthshire in 1947. A year later he was knighted.

Always interested in education, Rocyn Jones was determined to strengthen the bonds between Monmouthshire and South Wales. He was a member of the court of governors of the University of Wales and represented the university on the council of the Welsh National School of Medicine. He was also vice-president of the court of governors of the University College of South Wales and Monmouthshire.

He married in 1901 Alla, daughter of Alderman S. N. Jones, of Abertillery. She died in 1950. There were four sons of the marriage, one of whom was killed in Italy during the last war. His son, Gwyn, succeeded him as county medical officer of health of Monmouthshire in 1946, and his eldest son, Nathan, is an orthopaedic surgeon in Cardiff.

We are indebted to Dr. R. M. F. PICKEN, Provost of the Welsh National School of Medicine, for the following appreciation: The death of Sir David Rocyn Jones at the age of 80 was not unexpected, but it leaves a gap in the professional, administrative, and sporting life of South Wales and Monmouthshire which will not be filled. He was a man of very striking personality, strong views, and great courage. Those of us who were concerned both with the organized medical services and with university education saw a great deal of him throughout the past thirty years, especially in the councils of the Welsh National Memorial Association for the Prevention and Treatment of Tuberculosis, of the Cardiff Royal Infirmary, of the University College of South Wales and Monmouthshire, and of the Welsh National School of Medicine. He took a very prominent part in the discussions and negotiations leading up to the establishment of the Welsh National School of Medicine as an independent chartered institution in 1931. Although he was strongly opposed to the separation of the school from the university college—of which he was latterly senior vice-president—he supported its work loyally and vigorously after the severance took place. I look back with great pleasure and gratitude to the friendship and kindness which he always showed to myself, in spite of the fact that I might be regarded as one interested in the school's independence. His knowledge and experience of administrative procedure was invaluable to younger men, and he was sure to pounce on any breach of order or departure from orthodoxy. As president of the Welsh Rugby Union he did much to prevent any departure from clean amateurism and the best sporting spirit in football circles.

He was a strong supporter of everything which is fine in the Welsh way of life, but there was nothing narrow or parochial in this support. Indeed he always looked back with joy and appreciation to his young days as a student in Edinburgh, and for many years was the moving spirit in an association of old students in South Wales of that university. We of the profession in this area have watched the careers of his sons in medicine with great satisfaction, and extend to them our deepest sympathy in their bereavement.

W. P. writes: Sir David Rocyn Jones was a man with a unique collection of characteristics blended together, the sum total of which resulted in what is popularly called a "character." I knew and worked under him for twenty years—not that one ever worked under him; one worked with him. He was never "the boss" in the accepted sense

of the term, but was always referred to affectionately as "the Old Man." The welfare of his medical, nursing, and administrative staffs was always his primary concern, and anyone who attempted to interfere with this welfare did so at their peril. One never hesitated to consult Sir David about professional problems or private difficulties. During his period of office in Monmouthshire he built up a health and school medical service which earned a high reputation; in fact much of his pioneer work helped in the organization of the public health services generally. He was in all senses of the term progressive, and in some ways could be regarded as a visionary. His passing is mourned by countless friends both inside and outside the medical profession.

JAMES THOMSON, C.B., C.M.G., M.B., C.M.

Major-General James Thomson, who served with distinction in the Army Medical Services in the war of 1914–18, died at Aberdeen on April 17 at the age of 90.

James Thomson was born on July 15, 1862, and was educated at the University of Aberdeen, where he graduated M.B., C.M. in 1886. Immediately after graduation he entered the service of the Army Medical Department, becoming captain in 1887. He took part in the Nile Expedition of 1898, being awarded the British medal and the Khedive's medal, with clasp, and in the following year he was promoted major. By the time war broke out in 1914 he had attained the rank of lieutenant-colonel in the R.A.M.C., and thereafter he shouldered many heavy responsibilities. He was appointed C.B. in 1917 and C.M.G. in 1919, in which year he attained the rank of major-general. In 1918, after having been D.D.M.S. of 8th Corps, he was selected to succeed the late Major-General Sir William G. Macpherson as Deputy Director-General of Medical Services of the British Armies in France. After the war he became D.D.M.S. to General Sir Ivor Maxse, who was at that time commander-in-chief of Northern Command. Major-General Thomson, who was a Knight of Grace of the Venerable Order of St. John of Jerusalem, retired from the A.M.S. in 1920. He married Miss Mary E. Marr, daughter of Surgeon-Major G. Marr, I.M.S., in 1897.

We record with regret the death on March 21 from cerebral arteriosclerosis and thrombosis of Dr. W. F. CORFIELD. He was 73 years of age. Walter Francis Corfield was the younger son of the late Dr. W. H. Corfield, professor of hygiene, University College, London. From Westminster School he went on to study medicine at University College Hospital, where he qualified in 1904. After holding appointments as house-physician and assistant in the bacteriological laboratory at U.C.H. he graduated M.B., B.S. in 1907, and took the D.P.H. in the following year. He then travelled with a patient for about a year, and later became medical officer of health and school medical officer at Colchester, a post for which he was well suited and which he occupied with distinction. During the first world war he served in the R.A.M.C., attaining the rank of major. From 1924 to 1930 he served as secretary of the Essex Branch of the B.M.A., and he represented his Division at the annual meeting in Manchester in 1929. When he retired from his post in Colchester he became medical adviser to the Kuwait Oil Company: his capacity for organization and his training as an M.O.H. were most valuable in this work, which he liked and was interested in. During the course of his career Corfield wrote numerous articles for the medical journals covering a wide range of public health subjects. For about 20 years he spent his annual holiday at Lenzerheide, a Swiss ski-ing resort. He excelled at the old-fashioned telemark turn, and his knowledge and experience of the country and of snow conditions was exceptional. An active member of the Ski Club of Great Britain, he was at one time a judge for the second-class test. Corfield took his ski-ing and everything he did seriously, and was always on the lookout for an opportunity to improve his technique in other sports and games. He was a delightful companion, cheerful, calm, never angry, with a lively sense of humour, and he will be missed by a large number of friends. He leaves a widow.

Dr. ALBERT RILEY died suddenly at his home at Audley, Staffordshire, on December 27, 1952, at the age of 58. Albert Riley was born on October 24, 1894, the elder son of the late Mr. D. W. Riley, and was educated at the Newcastle Middle School, where he was head prefect and sports champion. After leaving school he took a post with the National Provincial Bank at Wakefield, Yorkshire, before joining the Forces and serving overseas with the King's Royal Rifles in the war of 1914–18. He was subsequently commissioned in the Cheshire Regiment and later transferred to the Royal Flying Corps. After demobilization he returned to his pre-war work for a time, and then decided to study medicine at the University of Manchester, where he graduated M.B., Ch.B. in 1924. After working as a ship surgeon for a time he settled in practice at Audley with the late Dr. William Megaw, eventually taking complete charge of the practice. Always a great lover of sport, his chief interest lay in cricket, and after he himself had ceased to play he became president of the Audley Cricket Club. He had all the attributes of the ideal family doctor, and will be remembered for many years in Audley. At the funeral on December 30 the parish church was filled with mourners who wished to pay their last respects to a greatly beloved physician. He is survived by his widow and one son.—J. L. B.

Dr. FREDERICK GILBERT LAUGHTON-SCOTT died at Tunbridge Wells on April 1, aged 66. His devotion to healing was of major importance in his life. From King's College, Canterbury, he went to Merton College, Oxford, with a classical scholarship, and his love of the classics and English literature remained with him throughout his life and gave him a humanity and breadth of vision which endeared him to both patients and friends. He studied medicine at Guy's Hospital, where he won an open scholarship in 1911, qualifying in 1914. During the 1914–18 war he served as a temporary surgeon in the Royal Navy, and on his return to England he did a considerable amount of work for the Ministry of Pensions on the treatment of shell-shock and allied conditions. He had an inquiring and critical mind and early in 1930 became interested in the rheumatic diseases. He cared intensely that his work should bring to medicine something in the nature of a genuine and recognized advance in therapeutics, and to this end he bent all his energies and lived to see his work on fibrositis accepted favourably. But his most outstanding characteristic that will be remembered for the longest time was his loyalty—a loyalty to the ethics of the profession, to his work, his patients, and to his many friends. This loyalty remained with him to the end of his last illness, borne with great courage and thought for others.—C. B. H.

The death occurred at Harrogate on April 5 of Dr. HUGH ROBERTSON at the age of 81, a few weeks after he had completed sixty years in medical practice. Hugh Robertson was born on August 7, 1871, and was educated at the University of Glasgow, where he graduated M.B., C.M. in 1893, proceeding to the M.D. in 1907. He was elected F.R.C.S.Ed. in 1899. After graduation Dr. Robertson was in practice at various places in Scotland, including Airdrie, Rutherglen, and Patna, in Ayrshire, where he was medical officer to the parish of Waterside. He moved to Harrogate in 1914, and for 26 years he was medical officer of Ashville and New College there. He also took an interest in local affairs and was a member of the town council from 1928 to 1935. A founder member and twice president of the Harrogate St. Andrew's Society, he was a great authority on Robert Burns and his work, and he was also an enthusiastic angler. Dr. Robertson, who was twice married, leaves a widow, and a daughter by his first marriage.—G. N. B.

Medical Notes in Parliament

PAY-BED REGULATIONS CRITICIZED

The new regulations relating to pay-bed accommodation in hospitals (S.I. 1953, No. 420) were discussed in the House of Commons on April 29, when Mr. A. BLENKINSOP, for the Opposition, moved a prayer for their annulment.

He said the broad effect of the regulations was to confirm recent increases in charges for amenity beds; to reduce pay-bed charges by sums which would vary even from hospital to hospital, according to very complex calculations that had to be made, but in general amounting to a reduction between 5 and 10%; and to provide for an increase in the maximum fees which could be charged by specialists giving treatment in pay-beds to their private patients.

He argued that pay-beds, although necessary initially to ensure that specialists should be broadly spread throughout N.H.S. hospitals, had always been an anomaly in the Health Service. These regulations, designed to ensure an increased use of pay-beds, would mean an increase in the sense of injustice among those who found themselves pushed further back in the queue for free treatment. They undoubtedly added to the specially favoured position of the part-time specialist in hospitals, as against the full-time specialist, ensuring that he should have more beds at his disposal as well as providing for additional maximum fees. Yet it was the part-time specialist whose service needed to be examined with some care in the Health Service. If there was room for cutting down expenditure it might well be there. It was the full-time specialist who on the whole gave the most economical service in the Health Service.

The pay-beds were not being fully used, and no doubt it would be said that they were too costly and these regulations were intended to ensure that they were more fully used and that the hospitals got more money. But large numbers of the beds were being sterilized for the use of specialists. In Stoke 55% of the pay-beds of the management committee were unoccupied, and the figures from Tyneside suggested a comparable proportion. The Minister, by these regulations, was encouraging the extension of a two-level service, one quality for those who could afford to pay, and a lower quality for others.

Mr. SOMERVILLE HASTINGS said that the Minister wanted these pay-beds used for ordinary patients when they were not occupied by paying patients, but the doctors thought otherwise—and they were on the spot. The doctors knew that only when they could get a patient into hospital at once, instead of having to wait three or four months, could they maintain and increase their private practices.

Mr. ANEURIN BEVAN said that in his initial discussions with the representatives of the Royal Colleges he was told that if he wished to keep the specialists at the hospital he must allow them to have their private patients there; otherwise there would be a direct encouragement to go to nursing-homes. He was extremely reluctant to agree, because he saw in it a grave breach of the general scheme. The medical profession was not entirely exempt from commercialism. Once the specialist was given the opportunity of having private patients in hospital he had a vested interest in increasing the number of private patients, which was exactly what happened. There was no justification, under proper administration, for a waiting-list at a hospital and empty beds in that hospital. The empty beds were kept there so that specialists could offer their patients who could afford to pay a bed at once. It could become a very evil racket.

Government Reply

Mr. IAIN MACLEOD, Minister of Health, replying to the discussion, pointed out that the schedule attached to the regulations remained broadly the same as that to the 1948 regulations, with the addition of certain new operations and procedures—for example, the development of fitting contact lenses. He had recently sent out, in conjunction with the regulations, guidance to hospitals. If the primary desire of a patient was for privacy, and it was a non-serious case, he should have his attention drawn to amenity beds if such existed in the hospital. Secondly, if his need for admission was urgent on medical grounds he had a right to be admitted, and there was again no need for the whole charges to be paid. Thirdly, if he desired a Section 5 bed it must be made absolutely clear to him—and there must be undertakings given in writing—that he understood in full the implications of what he was doing.

The object of these regulations was not to reduce the charge to private patients; it might have that result, but the object was to carry out fairly the 1946 Act. The 1948 regulations laid down that a standard daily charge, plus an average daily cost per in-patient representing medical care, plus various percentages, was to be the amount charged. It had been found that the regulations were trebly unfair. The percentages were now to be added to a sum which excluded the cost of paying medical staff. Secondly, they had been shown to be unfair because they included certain services which had little or no reference to the private block. Thirdly, they were unfair because the percentages had been found to be too high.

On the question of the new fees, he said that the fees had been unaltered since 1948, and in 1949 Mr. Bevan had agreed that they should be examined. That examination had taken place, and after consultations with the various consultant officers and the professions the new figures represented fairly general agreement. Hospital charges reflected actual costs, whereas medical fees had been subject to rigid ceilings since 1948, in spite of the fact that there had been enormous developments in medical technique since then.

The number of Section 5 beds at the latest count in February this year was 6,113, or 1.2% of all staffed beds. The number of Section 4 beds (part-payment) was 1.3%. So 97.5% of all beds in the Service were absolutely free. Compared with the end of 1950 those figures showed that there had been a decrease of 4.5% in Section 5 beds and an increase of 13% in Section 4 beds, while the free beds had increased by no fewer than 18,156, or 4.1%. In view of those figures no one could say that the present Government had taken advantage of Section 5 to multiply the number of pay-beds beyond what was conceived in the Act, or would do so.

No Word of Approval

It had been said that this was a new policy, and in some respects one in favour of the specialists. The best witnesses to call on that were the specialists. In the *British Medical Journal* of March 28* their joint committee commented on these regulations and his attitude towards them. He regretted to say that there was no word of approval for him throughout their comments. The specialists had wanted to abandon the detailed schedule. He had said, "No." They had wanted not a detailed price ceiling, but a few general ceilings within which they would adjust their amounts to the paying capacity of their patients. He had said, "Whatever might happen in the future, the time is not ripe for that." They had wanted a reduction straight away in the case of pay-beds. He had said, "That cannot be done without legislation, and I see no prospect of that." Those were the only three points on which he had interfered in these regulations, which had been prepared by the consultant officers of the Ministry.

Mr. BLENKINSOP asked what proposals the Minister had in mind to ensure that the empty beds were used for ordinary patients. Mr. MACLEOD said that he had called for a special report on the occupancy of these beds. The details were almost complete, and as soon as he had them he would be happy to discuss the matter.

The motion to annul the regulations was rejected by 261 votes to 233.

Supplement, March 28, p. 94.

BETTER MATERNITY BENEFITS

The National Insurance Bill, for which the Minister claimed that it made the most generous provision for motherhood yet provided, was given a second reading in the House

of Commons on April 29. It was stated during the debate that at the time the National Insurance Act, 1946—which it amends—came into operation there were 18,786 maternity beds in N.H.S. hospitals, and the most recent return was 19,369.

The point which attracted most attention was the introduction of the home confinement grant of £3, making for the first time a differentiation between the allowances to women who went to hospital and those who had their confinement at home. Fears were expressed that this might be an inducement to women who ought to go to hospital to remain at home for the sake of the extra money. Against that was quoted the report of the National Insurance Advisory Committee that representations had been made that the financial advantage under the present scheme of having the confinement in hospital was causing an excessive demand on maternity beds which ought primarily to be used for cases likely to need hospital attention.

Pharmaceutical Goods Prices

Mr. A. BLENKINSOP on April 30 asked the Minister of Health whether he was in a position to make a statement arising out of his discussions with manufacturers of pharmaceutical goods about the prices of proprietary brands. Mr. IAIN MACLEOD said that he could not at present, but added that this was a matter which was under very serious consideration by the Government.

Supplies to China

Mr. JOHN TILNEY on April 30 asked the President of the Board of Trade if he would make a statement in connexion with the supply of certain pharmaceuticals to China.

Mr. PETER THORNEYCROFT replied that pharmaceuticals were not subject to the embargo which the United Kingdom had maintained on certain exports to China ever since it was imposed by the previous Government after the United Nations resolution of May 18, 1951. Since August, 1951, however, exports to China of certain pharmaceuticals which would be of value to the maintenance of large military forces had been limited to normal civilian requirements. A number of Western European governments had hitherto permitted exports of these pharmaceuticals without restriction and this had tended to frustrate the controls which we have maintained. These governments had, however, now agreed to impose similar restrictions to ours.

Universities and Colleges

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on April 30, with the President, Sir Russell Brain, in the chair, the following were elected Fellows of the College: F. B. Byrom, M.D. (Australia); R. Jeremy, M.B. (Australia); A. T. Jones, M.D. (Cardiff); M. McC. Baird, B.M. (Canada); E. B. Brooke, M.B. (Carshalton); B. B. Bhatia, M.D. (India); T. F. McN. Scott, M.D. (United States); J. S. Harris, M.D. (Woodford Green); J. N. Cumings, M.D. (London); O. F. Thomas, M.R.C.P. (Liverpool); R. Knox, M.D. (London); J. MacD. Holmes, M.D. (Stafford); Mary J. Wilmers, M.D. (London); H. E. Holling, M.B. (London); Beryl D. Corner, M.D. (Bristol); G. Davison, M.D. (Cramlington); J. R. Forbes, M.D. (Flintshire); R. M. Kark, M.R.C.P. (United States); F. H. Kemp, M.B. (Oxford); S. Lazarus, M.D. (Glasgow); J. Smart, M.D. (London); J. F. Bromley, M.B. (Birmingham); Muriel J. L. Frazer, M.D. (Belfast); Sir William P. Mallinson, B.M. (London); H. G. Miller, M.D. (Newcastle-upon-Tyne); A. W. Woodruff, M.D. (London); W. W. Gooddy, M.D. (London); A. G. W. Whitfield, M.D. (Sutton Coldfield); D. I. Williams, M.B. (London); R. A. Henson, M.D. (London); Sir Frank Macfarlane Burnet, M.D., F.R.S. (Australia); J. F Fulton, M.D. (United States); G. L. Keynes, M.D., F.R.C.S., F.R.C.O.G. (London); and C. Laubry, M.D. (France).

Lord Horder was appointed delegate of the College to the annual cremation conference to be held at Llandudno from June 29 to July 1.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **April 18** (No. 15) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	18	2	8	0		24	2	9	0	1
Dysentery	282	33	88	6		489	63	34	2	1
Encephalitis, acute	3	0	0	0		2	1	1	0	
Enteric fever:										
Typhoid	2	0	0	0		1	0	0	1	
Paratyphoid	7	0	1(A)	0		13	0	0	0	
Food-poisoning	56	9		0		51	6		1	
Infective enteritis or diarrhoea under 2 years				21	19				14	10
Measles*	18,861	835	550	269	284	5,472	210	587	250	441
Meningococcal infection	54	6	11	1	4	44	2	12	1	4
Ophthalmia neonatorum	48	1	4	0		32	10	5	0	
Pneumonia†	796	57	473	14	8	680	49	291	16	1
Poliomyelitis, acute:										
Paralytic	26	1	1	0	2	14	2	2	1	
Non-paralytic	8	0				3	0			
Puerperal fever§	208	30	23	1		243	56	14	0	
Scarlet fever	994	67	151	35	51	1,134	93	158	9	35
Tuberculosis:										
Respiratory			147	27				134	34	
Non-respiratory			16	6				25	5	
Whooping-cough	2,847	181	374	40	152	2,306	129	183	77	42

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0		0	0	0		0	0
Dysentery	0	0				1	0			
Encephalitis, acute					0		1			0
Enteric fever	0	0	0			0	0			
Infective enteritis or diarrhoea under 2 years	8	1	1	3	0	15	1	6	0	1
Influenza	37	1	1	2	3	38	3	6	0	0
Measles		0	0		2		0	1	1	2
Meningococcal infection		0	0				2			
Pneumonia	300	33	26	19	11	284	42		16	5
Poliomyelitis, acute	8	1			0	2	0			0
Scarlet fever		0	0		0		0		0	0
Tuberculosis:										
Respiratory	119	19	14	4	6	139	20	19	5	16
Non-respiratory		2	2	3	3		5	4	1	2
Whooping-cough	3	0	1	0	1	2	0		0	0
Deaths 0–1 year	229	30	34	14	22	248	27	34	12	13
Deaths (excluding stillbirths)	5,428	731	623	126	209	5,828	823	645	98	173
LIVE BIRTHS	8,068	1175	923	235	409	6,887	1122	806	242	344
STILLBIRTHS	196	25	20			172	15	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

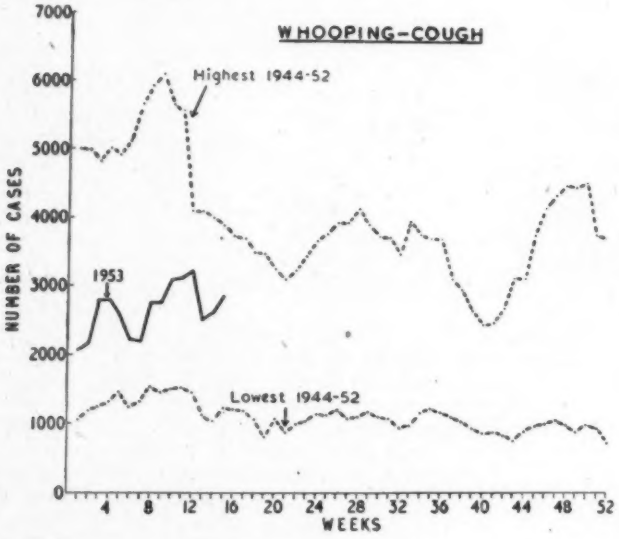
Cancer and Tuberculosis Deaths

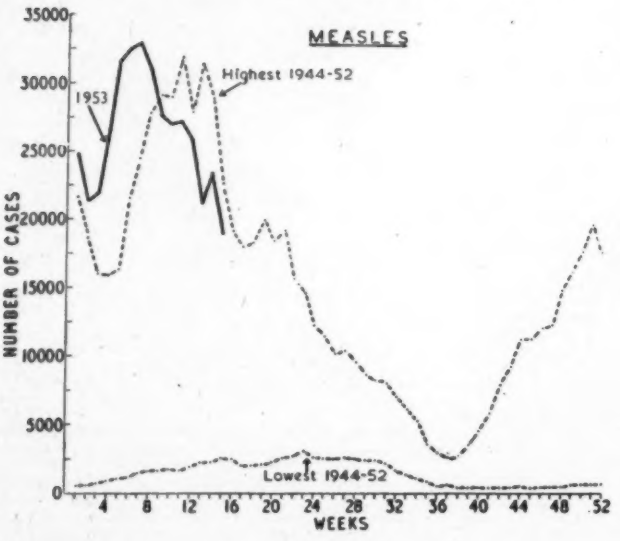
In England and Wales the provisional 1952 death rates for all forms of cancer were 2,149 and 1,850 per million population for men and women respectively. The 1951 figures were 2,120 and 1,822. The rise in the rate for men includes an increase from 530 to 567 per million population for deaths assigned to cancer of the lung and bronchus, making a total increase since 1947 of 47%.

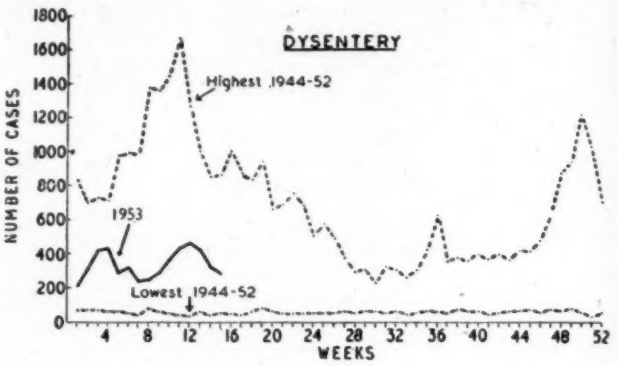
The provisional death rate for respiratory tuberculosis in 1952 was 212 per million persons. This is a decrease of 23% from the previous year, and is less than half the figure for 1947. The rate for other forms of tuberculosis was 28 per million persons, compared with 41 for 1951.

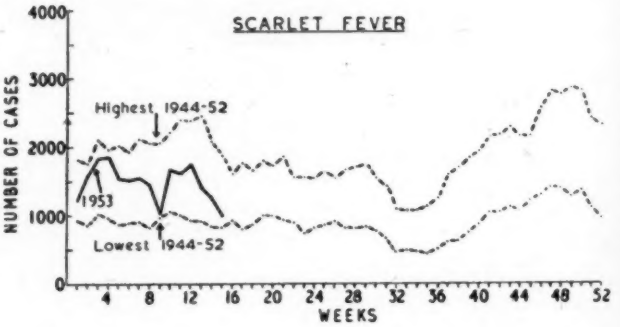
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ———. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending April 18 were falls of 4,527 in the number of notifications of measles, from 23,388 to 18,861, and 272 for scarlet fever, from 1,266 to 994, and a rise of 229 for whooping-cough, from 2,618 to 2,847.

The largest decreases in the local trends of measles were 490 in Yorkshire West Riding, from 1,896 to 1,406; 345 in Warwickshire, from 980 to 635; 245 in Essex, from 948 to 703; and 239 in Hertfordshire, from 627 to 388. The largest fall in the notifications of scarlet fever was 42 in Kent, from 70 to 28. The largest rises in whooping-cough were 93 in Lancashire, from 463 to 556, and 57 in Essex, from 136 to 193. 18 cases of diphtheria were notified, 1 less than in the preceding week.

34 cases of acute poliomyelitis were notified during the week. These cases were 2 fewer for both paralytic and non-paralytic cases than in the preceding week. The largest returns were Surrey 5 (Wimbledon M.B. 2) and Sussex 5 (Brighton C.B. 2).

282 cases of dysentery were notified, 43 fewer than in the preceding week. The largest returns were Lancashire 86 (Liverpool C.B. 36, Manchester C.B. 21, Preston R.D. 14), London 33, Leicestershire 28 (Leicester C.B. 28), and Middlesex 17 (Edmonton M.B. 12).

Week Ending April 25

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,047, whooping-cough 3,206, diphtheria 25, measles 13,731, acute poliomyelitis 41, dysentery 419, paratyphoid fever 8, and typhoid fever 2.

Infant Mortality Record

The infant mortality rate for England and Wales in 1952 fell to 27.6 per 1,000 related live births, the lowest ever recorded in this country. It was 2.0 below the rate for 1950, the previous lowest. Comparative rates in other countries were: In 1952, Sweden 20, Netherlands 23, U.S.A. 29; in 1951, New Zealand 23, Australia 25, Canada 38, France 51, Belgium 66, Italy 67.

On the basis of 1951 death rates, the estimated expectation of life of a male child at birth would be 65.8 years and that of a female child 70.9. These figures compare with 48.5 and 52.4 respectively in 1901.

The birth rate last year was the lowest recorded since 1941. There were 673,559 live births, representing a rate of 15.3 per thousand population. This was 0.2 below the rate for 1951. Of every thousand live births, 46 were illegitimate—5 per thousand fewer than the average for the preceding five years. The births registered in 1952 exceeded the deaths by 176,269; the corresponding excess for 1951 was 130,309 and the average excess for 1946–50 was 281,195.

Deaths during 1952 numbered 497,290, giving a rate of 11.3 per thousand population, compared with 12.5 in 1951 and 11.6 in 1950. This is the second lowest rate recorded in spite of a rate in the last quarter (12.4) which has been exceeded only twice since 1925.—*Quarterly Return for England and Wales*, fourth quarter of 1952.

The provisional maternal mortality rate (excluding abortion) per 1,000 live and stillbirths in England and Wales in 1952 was 0.59, a new low record. The previous lowest rate was 0.66 in 1951.

The provisional neonatal death rate (babies under 4 weeks of age) for last year was 18.9 per 1,000 related live births. In the previous year the rate was 18.8, and in 1939 it was 28.3.

Smallpox in the North Country

Up to noon, May 5, 27 confirmed cases of smallpox had been reported, including 7 deaths. There was 1 new suspected case in a soldier recently returned from Egypt. The new case reported since last week was a man aged 43, vaccinated in infancy.

Medical News

Royal College of Surgeons.—On May 5 the Queen laid a memorial stone to commemorate the first phase of the building operations at the Royal College of Surgeons. The ceremony took place in what will eventually be the Great Hall of the College. Enclosed in the stone is a casket containing copies of the College Calendar and other documents placed there by two postgraduate students from the residential college, Dr. H. Chesterfield Evans, of Brisbane, and Dr. C. B. Walker, of Ipswich. In his speech of welcome to the Queen the President of the College, Sir Cecil Wakeley, said that work was proceeding on the three new floors of museums, a gift from the Wellcome trustees, on the laboratories, and on the library. Work on the College of Surgical Science, presented by Lord Nuffield, was due to begin within a few months. The Bishop of London (Dr. Wand) dedicated the memorial stone and prayed for blessing on the new project. The President then presented the architect and representatives of the contractors to the Queen, who accepted from the architect a gold and tortoiseshell trinket-box belonging originally to George IV. After expressing the thanks of the College to her Majesty for laying the stone, Sir Cecil gave her a copy of Sir John Bland-Sutton's book, *The Story of a Surgeon*.

Minister's Committee on Health Service Costs.—Last week in the House of Commons the Minister of Health, Mr. Iain Macleod, announced the composition of the small independent committee of inquiry which he is asking to look into the costs of the Health Service. The chairman, as already noted (April 11, p. 840), is the Cambridge economist Mr. C. W. Guillebaud. The members are Professor J. W. Cook, F.R.S., regius professor of chemistry at Glasgow; Sir Geoffrey Vickers, V.C., a member of the National Coal Board and previously its legal adviser; Sir John Maude, formerly Permanent Secretary to the Ministry of Health; and Miss B. A. Godwin, a member of the General Council of the Trades Union Congress. The secretary is Mr. E. Halliday, of the Ministry of Health. The committee's terms of reference are: "To review the present and prospective cost of the National Health Service; to suggest means, whether by modifications in organization or otherwise, of ensuring the most effective control and efficient use of such Exchequer funds as may be made available; to advise how, in view of the burdens on the Exchequer, a rising charge upon it can be avoided while providing for the maintenance of an adequate Service; and to make recommendations."

British Occupational Hygiene Society.—A new society for the promotion of the science of occupational hygiene, the British Occupational Hygiene Society, was inaugurated last month at the London School of Hygiene and Tropical Medicine. The society's first president is Dr. T. Bedford, D.Sc., director of the Medical Research Council's Environmental Hygiene Research Unit, and the founder members include engineers, chemists, and physicists, as well as medical men, concerned with the maintenance of healthful conditions of work. The society will provide a forum where medical and non-medical workers in this field can share their experience. The honorary secretary is Mr. P. C. G. Isaac, lecturer in public health engineering, King's College, Newcastle-upon-Tyne.

Doctors and Sickness Insurance Schemes.—The International Social Security Association is preparing for discussions with the World Medical Association on the question of co-operation between the medical profession and sickness insurance institutions. According to the International Social Security Association, which represents institutions concerned with social security matters in 39 countries, this co-operation is not always as close as might be hoped. The problem is being discussed this week at a meeting in Düsseldorf.

The Radcliffe Infirmary.—Oxford University has reached agreement in principle with the board of governors of the United Oxford Hospitals for a new building plan on the Radcliffe Infirmary site which will strengthen the clinical school in two ways. First, the Nuffield professor of clinical medicine will have all his beds concentrated at the Radcliffe Infirmary instead of half at the Churchill Hospital. Secondly, the board of the faculty of medicine has recently recommended that the next Nuffield professor of surgery, to be appointed in succession to the late Sir Hugh Cairns, should for preference be a general surgeon. This is to be made possible by the provision of a new department, also in the Radcliffe Infirmary, with about 50 beds, operating-theatre, and laboratories. Temporary arrangements for increasing the number of beds at the Radcliffe Infirmary until the new building is complete are now being made by the board of governors.

Refresher Course for General Practitioners.—Some copies of the book, *Refresher Course for General Practitioners*, are still available. It comprises the first 55 articles printed in this popular *Journal* series. Each deals with a common problem of medical practice, and has been written (and fully revised) by an acknowledged authority. The price of the book is 25s. (post free). Orders should be sent to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Training of the Hospital Matron.—The King Edward's Hospital Fund for London is to run a 10-month residential course for prospective matrons and assistant matrons from the four Metropolitan Regions. The first course will start in September and be limited to 12 candidates. The sisters will live at 22, Holland Park, London, W.11. The course is a preparatory one, being designed primarily for the sister who shows promise of administrative ability, and the emphasis will be on the human aspects of management. The King's Fund already runs courses for ward sisters and for hospital administrators.

College of General Practitioners.—On April 30 the number of Foundation Members of the College was 1,911.

Nuffield Provincial Hospitals Trust.—The Investigation into the Functions and Design of Hospitals has moved from 33, Doughty Street, London, W.C.1, to the Trust's headquarters at Nuffield Lodge, Regent's Park, London, N.W.1 (telephone: Primrose 8871).

Professor W. T. J. Morgan, F.R.S., has been appointed deputy director of the Lister Institute of Preventive Medicine. Professor Morgan, who has been on the staff of the Lister Institute since 1928, is noted for his work on the chemistry of immunology.

Professor Joseph Gillman, head of the department of physiology at Witwatersrand University, has been awarded the South Africa Medal by the South African Association for the Advancement of Science. The South Africa Medal fund was instituted by members of the British Association in commemoration of their visit to South Africa in 1905.

Dr. F. I. Ashton has received the Queen's Commendation for Brave Conduct for his part in rescuing people trapped by the floods at Sutton-on-Sea, Lincolnshire.

COMING EVENTS

Symposium on Virology.—The Institut d'Hygiène et de Bactériologie at Lausanne has arranged a symposium on "Some Present Problems of Virology" to be held at Lausanne on May 22 and 23. Each paper will be followed by a discussion, and the papers will be read in either English or French. The fee for the symposium is 15 Swiss francs. Further information may be obtained from Professor Hauduroy, 19, rue César Roux, Lausanne.

Liverpool Medical Exhibition.—The 1953 Liverpool Medical Exhibition is to be held at St. George's Hall, Liverpool, from May 18 to 22. The exhibition, which will be open from 11 a.m. to 6.30 p.m. daily, will be opened by Dr. E. Noble Chamberlain.

British Empire Leprosy Relief Association.—The annual general meeting of the British Empire Leprosy Relief Association will be held in the Conference Room, Church House, Great Smith Street, London, S.W.1, on May 21 at 3 p.m. The chair will be taken by the Rt. Hon. Oliver Lyttelton, who will deliver the main lecture. Dr. Robert Cochrane will speak on the treatment of leprosy.

Ross Institute of Tropical Hygiene.—The Ross Institute Industrial Advisory Committee will hold an open meeting in the council chamber of the Rubber Growers' Association, 19, Fenchurch Street, E.C.3, on May 21 at 2.15 p.m. The subjects for discussion will include "Tropical Health Problems and Their Connexion with Industrial Relations," "International Health Work," and "Malaria in Malaya."

Cancer and the Viruses.—Dr. Pierre Lépine, Director of the Virus Research Department of the Institut Pasteur, Paris, will speak at the Institut Français, 15, Queensberry Place, London, S.W.7, on May 12 at 6 p.m. The subject of his address, which will be given in French, will be "Le problème du cancer dans ses relations avec les virus."

Bart's Exhibition.—St. Bartholomew's Hospital, E.C.1, is holding an exhibition of its historical documents and other treasures from May 14 to 16. The exhibition will be open to the public each day from 10.30 a.m. to 6.30 p.m., and visitors should enter through the main gate in West Smithfield.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, May 11

INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture-demonstration by Dr. E. Stengel.

MEDICAL SOCIETY OF LONDON.—8.45 p.m., Annual Oration by Sir Russell Brain, P.R.C.P.: Need for a Philosophy of Medicine.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. H. S. Banks: Coliform Infection in Gastro-enteritis.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor H. R. Dew: Post-operative Intravascular Thrombosis.

ROYAL EYE HOSPITAL.—5 p.m., Professor Arnold Sorsby: Diseases of Metabolism and their Ocular Signs.

ST. ANDREWS UNIVERSITY.—At Surgery Lecture Theatre, Dundee, 5 p.m., Sir W. Heneage Ogilvie: Problems of the Gastro-oesophageal Junction.

UNIVERSITY COLLEGE.—At Physiology Theatre, 4.45 p.m., Sir Rudolph Peters, F.R.S.: Inhibitors and Intracellular Chemical Dissection.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal Society of Medicine, 8.30 p.m., Cavendish Lecture by Viscount Simon: The Doctor in the Witness Box.

Tuesday, May 12

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 7 for 7.30 p.m., annual dinner.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor J. Chassar Moir: Use of Radiology in Labour.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Moynihan Lecture by Dr. R. B. Cattell (Boston): Extra Hepatic Obstruction of the Bile Ducts.

ROYAL EYE HOSPITAL.—5 p.m., Mr. T. M. Tyrrell: Surgery of Glaucoma and its Complications.

ST. ANDREWS UNIVERSITY.—At Surgery Lecture Theatre, Dundee, 5 p.m., Sir W. Heneage Ogilvie: Pitfalls in Surgical Diagnosis.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School.—5 p.m., Almroth Wright Lecture by Dr. J. G. Davis, D.Sc.: Some Public Health Aspects of Milk.

Wednesday, May 13

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., Miss Sybil Campbell (Metropolitan Magistrate): A Day in the Life of a Metropolitan Magistrate—with Particular Reference to Problems of Punishment.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor A. Frazer: Disordered Function of the Small Intestine.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. R. J. Ludford: Tissue Cultures—Malignant Growth.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. L. H. Savin: Ophthalmic Neurology.

Thursday, May 14

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Dr. D. S. MacPhail: Psychotherapy for Criminals.

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., annual general meeting; 8.30 p.m., 32nd Silvanus Thompson Memorial Lecture by Dr. L. H. Gray, Ph.D.: Initiation and Development of Cellular Damage by Ionizing Radiation.

CAMBRIDGE UNIVERSITY.—At Senate House, 5 p.m., Rede Lecture by Professor A. D. Gardner: The Proper Study of Mankind.

●HAMPSTEAD GENERAL HOSPITAL.—3 p.m., Mr. G. Qvist: Vascular Disease of Limbs; 4.15 p.m., Dr. M. Kremer: Epilepsy.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. C. F. Rolland: Diabetes in Pregnancy.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Mycology—Structure of Pathogenic Fungi and their Identification.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Mr. A. W. Bourne: Hypertension in Pregnancy and its Prognosis.

LONDON UNIVERSITY.—At Guy's Hospital Medical School, 5 p.m., Dr. N. G. Emmelin (Lund): Secretion of Saliva.

NUFFIELD ORTHOPAEDIC CENTRE, Wingfield-Morris Orthopaedic Hospital.—8.30 p.m., Mr. P. Wiles: Posture.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. G. E. Burch (Louisiana): Vectorcardiography.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Surgeon Commander F. Ellis, O.B.E., R.N.: Desirable and Tolerable Levels of Warmth in Warm Climates (with special reference to the requirements of men in the Royal Navy).

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Non-Paralytic Strabismus: Care and Treatment of the Squinting Child.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor G. Gustafson (Sweden): Modern Methods in Dental Histology.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. A. S. Paterson: postgraduate demonstration in neurology.

Friday, May 15

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 2.15 p.m., Diagnosis Section Meeting. Dr. R. Astley: Tricuspid Atresia; Dr. D. E. Truscott: Radiological Control of Kidney Injuries; Dr. P. G. Keates: Some Physiological Observations Made During Excretion Urography; Dr W. Horrer Smith: Reliability of Excretion Urography in the Diagnosis of Bladder Tumours.

●GUY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Fison Memorial Lecture by Sir Lawrence Bragg, F.R.S.: *X*-ray Analysis of Protein Molecules.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. T. Brain: Common Skin Diseases in Children.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Dr. J. N. Morris: History of Social Medicine.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Dr. R. B. Cattell (Boston): Advances in Pancreatic Surgery.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. John Bruce: Hazards of Major Surgery.

●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor A. Frazer: Disordered Functions of the Small Intestine.

●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5 p.m., William Blair-Bell Memorial Lecture by Dr. Henry Roberts: Observations on Micturition in the Female.

ST. ANDREWS UNIVERSITY.—At Surgery Lecture Theatre, Dundee, 5 p.m., Sir W. Heneage Ogilvie: Independence and Authority in Medical Practice.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Obstetric and Gynaecological Conference. Mr. H. C. Hanley: Urological Problems During Pregnancy.

Saturday, May 16

BIOCHEMICAL SOCIETY.—At Department of Physiology, Medical School, Hospitals Centre, Birmingham, 1.45 p.m., scientific papers.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 11 a.m., Professor W. C. W. Nixon: Disordered Uterine Action.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

A Heavily Furred Tongue

Q.—*How should a man of 40 with a persistently and heavily furred tongue be investigated and treated? The condition started 6 months before an operation for appendix abscess 14 years ago, and has only remitted once since—during the month immediately after operation. The patient also suffers from buccal ulcers and flatulence and distension after meals occasionally. There is no evidence of local sepsis. All the teeth have been removed in an effort to cure the condition.*

A.—It is not always easy to account for a furred tongue. It only occasionally produces symptoms, and these then seem to be made worse by worrying. It is important to see that the patient is taking a normal diet, not slops, and that he is not smoking or drinking to excess. Nasal obstruction should be excluded, and likewise constipation or the excessive use of aperients. The coexistence of a furred tongue, flatulence, and distension suggests the syndrome of reverse peristalsis. This is usually due to an irritable focus in the alimentary tract or a reflex disturbance from elsewhere. It would be well to begin investigation by an *x*-ray examination of the gall-bladder, as this may have been infected at the same time as the appendix. If this is normal the patient should have a barium meal and follow-through, with particular reference to the possibility of a lesion in the lower ileum. A test meal may be done to exclude achlorhydria. Finally, a gastroscopy may be performed to look for gastritis, though it will prove difficult to treat it if it is found.

Repeated Failure of Lactation

Q.—*A healthy woman of 27, now in her third pregnancy, has with her previous two children had considerable difficulty with breast-feeding. Despite all the usual measures taken after delivery, the supply of milk has been inadequate on both occasions and has had to be supplemented very extensively within the first few weeks. There seems to be no psychological difficulty and she is anxious to feed the new baby. She is now 25 weeks advanced in pregnancy, and, although the breasts are enlarged, no secretion can be expressed from the nipples. Are there any measures which can be taken during the pregnancy to increase the supply after delivery?*

A.—There are some women who, despite all treatment, fail to lactate in successive pregnancies, and in these it is assumed that there is a failure of development of gland tissue or some inherent fault which prevents the breast responding to the various factors which determine lactation after childbirth. For this minority little can be done. The majority of women, however, can breast-feed satisfactorily given the determination to do so, proper management, and a lusty child with a good sucking reflex.

In the case described the only treatment necessary at present is to ensure that the woman has a good diet, protein being especially important. As pregnancy progresses attention should be paid to the nipples to see that they project well. Thereafter it would probably be best to follow the scheme advocated by H. K. Waller. This includes daily massage of the breasts with deliberate expression of colostrum during the last six weeks of pregnancy. After labour, engorgement of the breasts should be treated with small doses of stilboestrol for 24 to 48 hours. As lactation becomes established the breasts should be "stripped" after each feed—that is, they should be completely emptied by manual expression.

Drug treatment to increase the supply of milk is generally unsatisfactory. There would be no harm, however, in giving for five to seven days either thyroid 6 to 10 gr. (0.4 to 0.65 g.) daily, or Lugol's iodine 6 minims (0.35 ml.) twice daily, starting on the fifth day of the puerperium.

Combined Diphtheria–Pertussis Inoculation

Q.—*At what age do the experts advise that a combined diphtheria–pertussis inoculation should be given?*

A.—It is assumed in this question that a combined diphtheria–pertussis prophylactic is already accepted as safe and effective as well as being administratively convenient. In regard to safety, there is some evidence that the slight risk of post-inoculation poliomyelitis, which may accompany injections in areas where poliomyelitis is prevalent, is particularly associated with an alum-containing diphtheria–pertussis mixture. This risk may be lessened by using a mixture of diphtheria toxoid and pertussis vaccine without alum, although there are as yet no published data on this point. As regards effectiveness, experimental and field studies indicate that the antigenic potency of diphtheria toxoid is not adversely affected, and may be enhanced, by mixture with pertussis vaccine. Whether this mixture affects the antigenic value of the pertussis vaccine is less certain.

If and when the combined prophylactic is shown to be both safe and effective there will be arguments for and against inoculating children either in the first six months or in the second six months of life. In favour of early inoculation, say from three months onwards, is the fact that 5–10% of children develop whooping-cough in the first year of life, and about two-thirds of the deaths from whooping-cough occur in this age group. On the other hand, it is not known if children are as well protected by pertussis immunization in the early months of life as they are when they receive the vaccine rather later. There is the further risk in diphtheria immunization that children of 3 to 6 months of age may still have some diphtheria antitoxin passively transferred from the mother, and this antibody may interfere with the child's response to the diphtheria prophylactic. In view of these considerations it might be advisable to begin immunization with a combined prophylactic around 6 months of age, and give a reinforcing dose 2–3 years later. Until the combined prophylactic has been proved to be safe and effective, pertussis immunization (three monthly doses) could be begun at 3 to 4 months and diphtheria immunization at 6 to 8 months of age. Obviously, no advice can be given about the best combined prophylactic at this stage.

Prognosis in Pneumoconiosis

Q.—*What is the prognosis in pneumoconiosis and the likelihood of tuberculosis supervening?*

A.—The word "pneumoconiosis" covers such a multitude of differing pathological and clinical conditions that it is impossible to answer the simple question that is asked. In cases of acute silicosis arising in the abrasive soap industry, death has occurred within three years of first exposure,[1] and patients with beryllium and aluminium pneumoconiosis have died 3 years and 18 months respectively from first exposure.[2,3] At the other extreme, aged miners may be found to have advanced pneumoconiosis which must have originated during their work anything up to 60 years previously, and the milder forms of any pneumoconiosis may be compatible with a normal span of life. Life tables for a miscellaneous group of cases of simple pneumoconiosis and silico-tuberculosis are given by Turner and Martin[4] and for certified coal-miners by Stewart.[5] The prognosis of coal-miners with pneumoconiosis is also discussed by Berard, Martin, Ode, and Roche[6] and that of a miscellaneous group of silicotics by Baldi.[7] From these papers it emerges that cases of these kinds of simple pneumoconiosis have a prognosis not very greatly different from that of the ordinary

population so long as their pneumoconiosis does not become complicated by tuberculosis, when the prognosis is much worse. The more rapid the onset of pneumoconiosis, and usually, therefore, the younger the man, the greater the liability of conversion at some time to silico-tuberculosis and the worse the prognosis. Cases with "massive fibrosis" have a worse prognosis, and cases with open tuberculosis seldom live more than two years. The liability to develop open tuberculosis appears to be much greater in cases of pure silicosis than in the various forms of mixed dust pneumoconiosis such as those of coal-workers and foundry workers. This is shown by the much higher tuberculosis death rates that have prevailed in the pure silica risk industries than in coal-mining and foundries. Other forms of pneumoconiosis than silicosis—for example, asbestosis, aluminosis, beryllosis—do not appear to predispose to tuberculosis.

The frequency with which tuberculosis is found to complicate pneumoconiosis depends upon the diagnostic criteria and upon the material used for the study. For instance, in post-mortem examinations of coal-miners Rogers[3] found tuberculosis in 75.8% of cases with massive fibrosis, Gooding[7] found it in 26% of all cases. Theodos and Gordon[10] found a positive sputum in 13% of coal-miners admitted to hospital, whereas in a community survey in a coal-mining district Cochrane (unpublished) found that only 1% of all cases of massive fibrosis had a positive sputum. The diagnosis of tuberculosis on the grounds of a positive sputum is the only way of making the diagnosis certain. When clinical and radiological criteria are also admitted, the proportion of cases of pneumoconiosis with tuberculosis will be found to range from about 5% to 75%, depending upon the selection of cases and the diagnostic whim of the observer.

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6 *Sem. Hôp. Paris*, 1949, **25**, 507.
7 *Med. d. Lavoro*, 1952, **43**, 147.
8 *Lancet*, 1946, **1**, 462.
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Shortening the List of Notifiable Diseases

Q.—*Can a local authority shorten the list of diseases notifiable in its area as well as lengthen it?*

A.—"Notifiable disease" is defined by section 343 of the Public Health Act, 1936, as any one of nine named diseases, plus any infectious disease which the local authority (with the approval of the Minister) may declare to be a notifiable disease within its area.

A local authority has no power to shorten the list of named diseases, but only those which became notifiable by a resolution of its own council. To remove such a disease from its list a further resolution of the council is required and also the approval of the Minister.

In addition, the Minister has power to make regulations under section 143 of the Public Health Act, 1936, for the treatment of persons affected with any epidemic, endemic, or infectious diseases, and for preventing the spread of such diseases. These regulations include provisions requiring notification of the diseases to which they apply, and may extend to the whole of England and Wales or any part thereof. Regulations made by the Minister may of course be amended or revoked by him.

Eosinophils in C.S.F.

Q.—*What are the causes of eosinophilia in the C.S.F.?*

A.—Very little is known about the incidence of eosinophils in the cerebrospinal fluid, and less still about their significance. Only rarely are these cells seen, and then mainly in cerebral syphilis and in some cases of acute meningitis, always provided there has been no blood admixture. Eosinophils might also be found in the C.S.F. in allergic conditions.

NOTES AND COMMENTS

Implantation of Hormone Pellets.—Dr. R. P. EDKINS, Ph.D. (Pharmaceutical Research Department, Organon Laboratories, Motherwell, Lanarks), writes: With regard to the previous notes on this matter (February 28, p. 519, and March 14, p. 632) it must, as Mr. A. R. G. Chamings states, be regarded as dangerous to boil these pellets, as most of the hormone substances used soften or actually melt under this treatment, and at the best the pellets will become deformed. A simple and invariably successful method by which either fused or compressed pellets which have been accidentally contaminated may be resterilized without fear of melting or distortion consists in keeping the pellets in a solution of phenol (0.5%) or phenylmercuric nitrate (0.002%) or other substance having similar bactericidal activity, at a temperature not below 37° C. or above 80° C. for 24 hours; the addition of a small percentage of a surface active agent such as cetrimide (0.025%) to the phenol solution (or other bactericide, provided there is no reaction between them) is an added advantage, as it promotes efficient wetting of the surface of the pellet. After this treatment, the pellet may then be implanted directly, after preliminary drying, if desired, on a sterile towel. It must be realized that this treatment will sterilize only the external surface of the pellet; but, since it is internally sterile by the process of manufacture, it is only the outer surface which will require resterilization if the pellet is accidentally contaminated. It is emphasized that it is undesirable to apply this process to pellets which have already been implanted and which have either been removed intentionally or extruded.

Poisonous Snakes.—Sir HAROLD SCOTT (Braintree) writes: Your expert in his reply on the treatment of bites by poisonous snakes ("Any Questions?" April 4, p. 793) rightly stresses the specificity of antivenins. As the use of such is generally urgent and they may not be immediately obtainable, a first-aid treatment which will delay the action of the poison deserves to be more widely known. Almost 30 years ago (in 1924) the fact was observed that soaps could detoxify snake venoms, and in 1945 Ahuja and Brooks in India showed that local injections, at four or five points surrounding the site of the bite, each of 0.5–1 ml. of 5% emulsion of "lifebuoy" carbolic soap (say to a total of 5 ml.) might delay the action of the poison for some hours, at least two and often more. Carbolic soap is to be found in many houses, and it might be kept made up in a 5% strength at local dispensaries in countries where snake-bites are likely to occur. Bleeding should be encouraged by crucial incisions.

OUR EXPERT writes: I agree that local injection of soap emulsion in the region of the bite might be worth trying in an emergency, but it should be stressed that it is only a first-aid treatment, and should never be regarded as a substitute for antivenin. The idea of using soap suspension in this way arose from some work on the effect of surface-tension suppressants on tissue poisons, including bacterial toxins and certain snake venoms. It has since been shown that soaps, particularly those of the unsaturated fatty acids, have some retarding effect on the venoms of rattlesnake, asp, cobra, krait, and ringhals. This effect has been shown both *in vitro* and *in vivo* in laboratory animals, including pigeons. I believe that the injection of carbolic soap emulsion has recently been used by Ahuja and Brooks as first-aid treatment of snake-bite in man. I am grateful to Sir Harold Scott for raising this point, which perhaps should have been included in my reply to the original question.

Corrections.—The figure for Foundation Membership of the College of General Practitioners given in the legend to the map in the *Journal* of May 2 (p. 990) should have read 1,807.

In the article entitled "Controlled Hypotension in Neurosurgery with Hexamethonium and Procaine Amide" (May 2, p. 961) by Dr. David Aserman, acknowledgment was inadvertently omitted to the fact that the procaine amide used in the investigation was generously supplied by Messrs. E. R. Squibb and Sons.

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